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Ran et al.

(10) **Patent No.: US 11,370,762 B2**
(45) **Date of Patent: Jun. 28, 2022**

- (54) **VINYLAENE DERIVATIVE AND APPLICATION**
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- (73) Assignee: **SHENYANG RESEARCH INSTITUTE OF CHEMICAL INDUSTRY CO., LTD.**, Liaoning (CN)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **16/489,815**

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(51) **Int. Cl.**
A61P 35/00 (2006.01)
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C07C 233/55 (2006.01)
C07C 275/40 (2006.01)
C07C 275/42 (2006.01)
C07C 335/22 (2006.01)

(52) **U.S. Cl.**
CPC **C07D 257/04** (2013.01); **A61P 35/00** (2018.01); **C07C 233/55** (2013.01); **C07C 275/40** (2013.01); **C07C 275/42** (2013.01); **C07C 335/22** (2013.01)

(58) **Field of Classification Search**
CPC A61P 35/00; C07D 257/04; C07C 233/55; C07C 275/40; C07C 275/42; C07C 335/22

See application file for complete search history.

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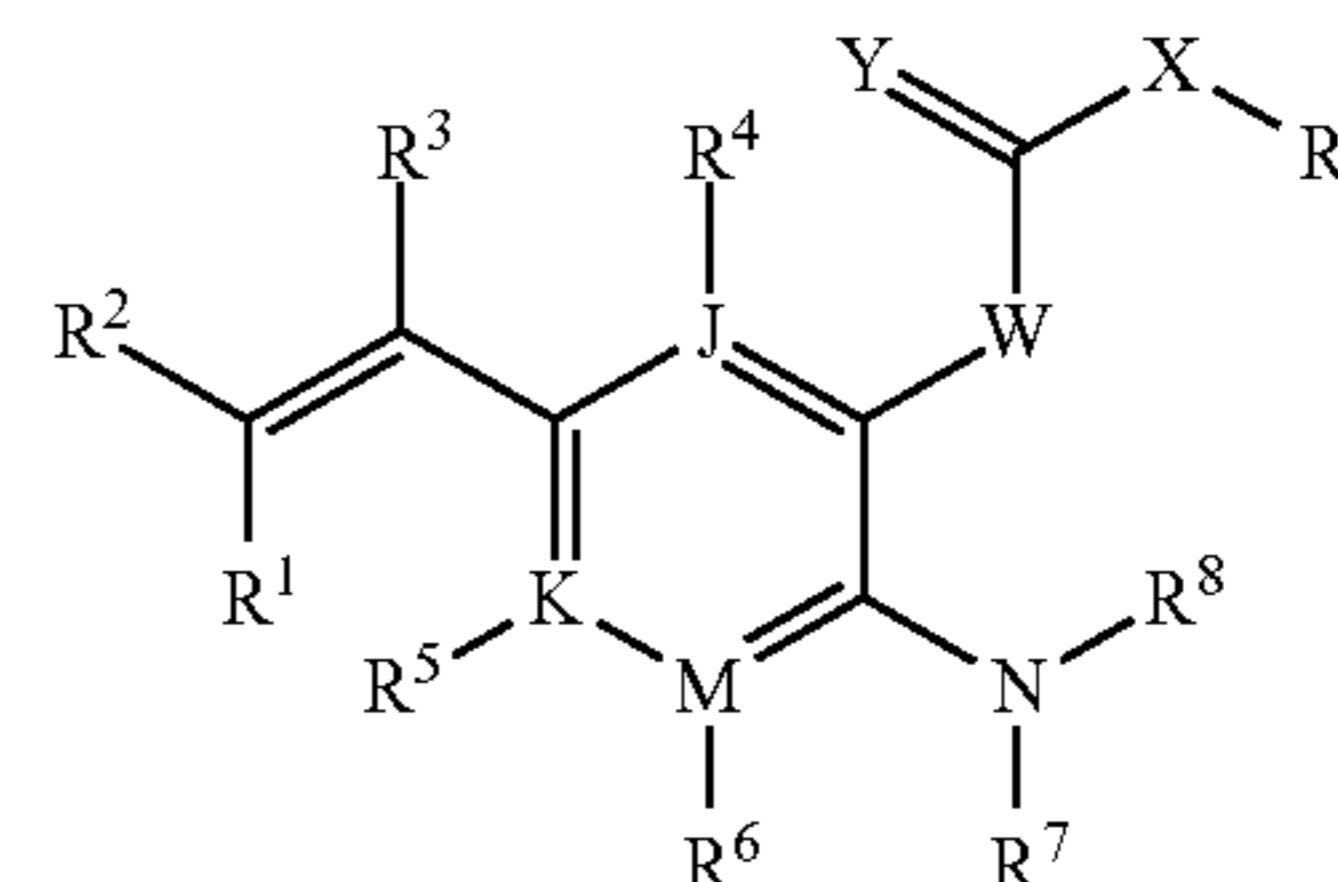
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(57) **ABSTRACT**

The present invention relates to a vinylarene deriv. which modulates or inhibits the enzymic activity of indoleamine 2,3-dioxygenase 1 (IDO-1), and the use thereof, and further relates to a vinylarene deriv. and the use thereof. The vinylarene deriv. and its stereoisomer, cis- or trans-isomer, or tautomer thereof and pharmaceutically acceptable salt thereof, has an IDO-1 enzyme inhibitory activity, and is expected to provide brand new therapeutic methods and schemes for related diseases caused by IDO enzymes.



I

3 Claims, No Drawings

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VINYLARENE DERIVATIVE AND APPLICATION

FIELD OF THE INVENTION

The invention relates generally to compounds vinylarene derivative that modulate or inhibit the enzymatic activity of indoleamine 2,3-dioxygenase 1 (IDO-1) and its application, further vinylarene derivative and its application.

BACKGROUND OF THE INVENTION

Indole-2,3-dioxygenase (IDO) is a heme-containing intracellular enzyme that catalyzes the first and rate-determining step in the degradation of amino acid L-tryptophan. IDO catalyzes the essential amino acids L-tryptophan to N-formyl kynurenine and cleans up L-tryptophan in humans. By degrading tryptophan, IDO causes a microenvironment in which tryptophan is absent in the body, which in turn leads to a variety of diseases related to tryptophan deficiency such as cancer, viral infection, depression, organ transplant rejection or autoimmune diseases. Therefore, in recent years, the research of high-efficiency IDO inhibitors has become a hot research in drug development.

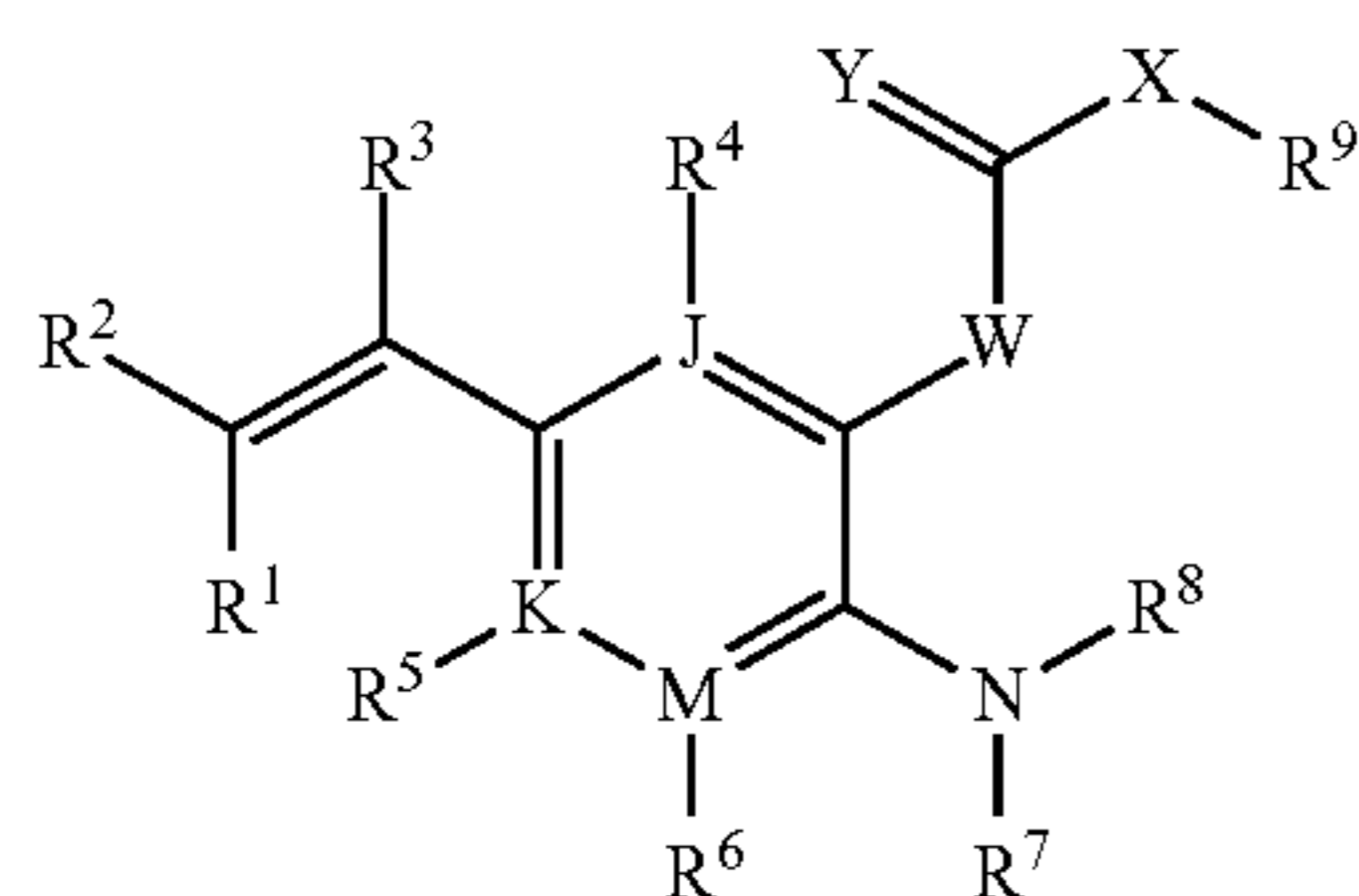
There are no IDO-1 inhibitors were approved for listing, and the diseases associated with IDO-1 enzymes still lack treatment methods and treatment options. The development of IDO-1 enzyme inhibitors has a huge potential market.

SUMMARY OF THE INVENTION

The purpose of the invention is to provide a compound which modulates or inhibits the enzymatic activity of IDO and/or a pharmaceutically acceptable salt, its stereoisomer, cis-trans isomer and a tautomer, and a method which modulates or inhibits IDO-1 enzymatic activity, and an application of the compound for the preparation of pharmaceutical.

In order to achieve the above purposes, the technical scheme adopted by the present invention is as follows:

The present invention is a vinylarene derivative as a regulator or inhibitor of indoleamine-2,3-dioxygenase (IDO-1). The aromatic ethylene derivative is a compound shown in formula I, its stereoisomer, cis-trans isomer, tautomer and pharmaceutically acceptable salt thereof.



wherein

W is selected from CH₂, O or NH;
 X is selected from CH₂, O or NH;
 Y is selected from O or S;
 J is selected from N or C;
 K is selected from N or C;
 M is selected from N or C;
 R¹ and R² are selected from H, COOH, CONHR¹⁰, —CONHSO₂R¹⁰, COOR¹⁰, C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl;

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R³ is selected from H, C₁-C₁₂ alkyl, halo C₁-C₁₂ alkyl, C₂-C₂ alkenyl, halo C₂-C₁₂ alkenyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl;

R⁴ is selected from H or halogen;

R⁵ is selected from H or halogen;

R⁶ is selected from the group consisting of H, halogen, nitro, cyano, C₁-C₁₂ alkyl, C₃-C₁₂ cycloalkyl, C₃-C₁₂ heterocycloalkyl, halo C₁-C₁₂ alkyl, C₁-C₁₂ alkoxy, halo C₁-C₁₂ alkoxy, C₁-C₁₂ alkoxy C₁-C₁₂ alkyl, halo C₁-C₁₂ alkoxy C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₃-C₁₂ cycloalkenyl, halo C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, halo C₂-C₁₂ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₁₂ alkyl, heteroaryl C₁-C₁₂ alkyl, aryl C₁-C₁₂ alkoxy, heteroaryl C₁-C₁₂ alkoxy, aryloxy or heteroaryloxy;

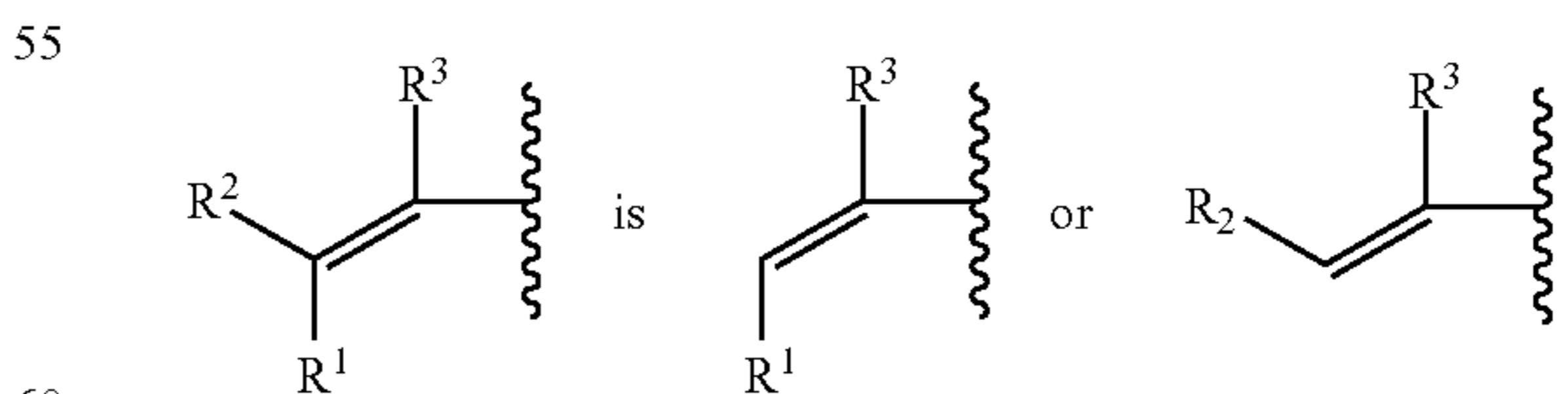
R⁷ and R⁸ are the same or different and selected from the group consisting of H, C₁-C₁₂ alkyl, C₃-C₁₂ cycloalkyl, C₃-C₁₂ heterocycloalkyl, halo C₁-C₁₂ alkyl, C₁-C₁₂ alkoxy C₁-C₁₂ alkyl, halo C₁-C₁₂ alkoxy C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₃-C₁₂ cycloalkenyl, halo C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, halo C₂-C₁₂ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₁₂ alkyl, heteroaryl C₁-C₁₂ alkyl;

R⁹ is selected from the group consisting of H, C₁-C₁₂ alkyl, C₃-C₁₂ cycloalkyl, C₃-C₁₂ heterocycloalkyl, halo C₁-C₁₂ alkyl, C₁-C₁₂ alkoxy, halo C₁-C₁₂ alkoxy, C₁-C₁₂ alkoxy C₁-C₁₂ alkyl, halo C₂-C₁₂ alkoxy C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₃-C₁₂ cycloalkenyl, halo C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, halo C₂-C₁₂ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₁₂ alkyl, heteroaryl C₁-C₁₂ alkyl;

R¹⁰ is selected from the group consisting of C₁-C₁₂ alkyl, C₃-C₁₂ cycloalkyl, halo C₁-C₁₂ alkyl, halo C₃-C₁₂ cycloalkyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₁₂ alkyl, heteroaryl C₁-C₁₂ alkyl;

R¹¹ is selected from the group consisting of H, halogen, nitro, cyano, C₁-C₁₀ alkyl, halo C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, halo C₁-C₁₀ alkoxy, C₁-C₁₀ alkylthiol, C₁-C₁₀ alkylcarbonyl, C₁-C₁₀ alkoxy carbonyl, C₂-C₁₀ alkenyl, halo C₂-C₁₀ alkenyl, C₃-C₁₀ alkenyloxy, halo C₃-C₁₀ alkenyloxy, C₂-C₁₀ alkynyl, halo C₂-C₁₀ alkynyl, C₃-C₁₀ alkynyloxy, halo C₃-C₁₀ alkynyloxy, halo C₁-C₁₀ alkylthiol, halo C₁-C₁₀ alkylcarbonyl, C₁-C₁₀ alkylamino, halo C₁-C₁₀ alkylamino, C₂-C₁₀ dialkylamino, C₁-C₁₀ alkylcarbonylamino, halo C₁-C₁₀ alkylcarbonylamino, C₁-C₁₀ alkylaminocarbonyl or halo C₁-C₁₀ alkylaminocarbonyl.

The compound of the formula I, its stereoisomers, cis-trans isomers, tautomers and pharmaceutically acceptable salts thereof, the more preferred compounds of the formula are:



W is selected from CH₂, O or NH;

X is selected from CH₂, O or NH;

Y is selected from O or S;

J is selected from N or C;

K is selected from N or C;

M is selected from N or C;

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R¹ and R² are selected from the group consisting of COOH, CONHR¹⁰, —CONHSO₂R¹⁰, COOR¹⁰, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl;

R³ is selected from the group consisting of H, C₁-C₆ alkyl, halo C₁-C₆ alkyl, C₂-C₆ alkenyl, halo C₂-C₆ alkenyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl;

R⁴ is selected from H or halogen;

R⁵ is selected from H or halogen;

R⁶ is selected from the group consisting of H, halogen, nitro, cyano, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ heterocycloalkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy, halo C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, halo C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkenyl, halo C₂-C₆ alkenyl, C₂-C₆ alkynyl, halo C₂-C₆ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₆ alkyl, heteroaryl C₁-C₆ alkyl, aryl C₁-C₆ alkoxy, heteroaryl C₂-C₆ alkoxy, aryloxy or heteroaryloxy;

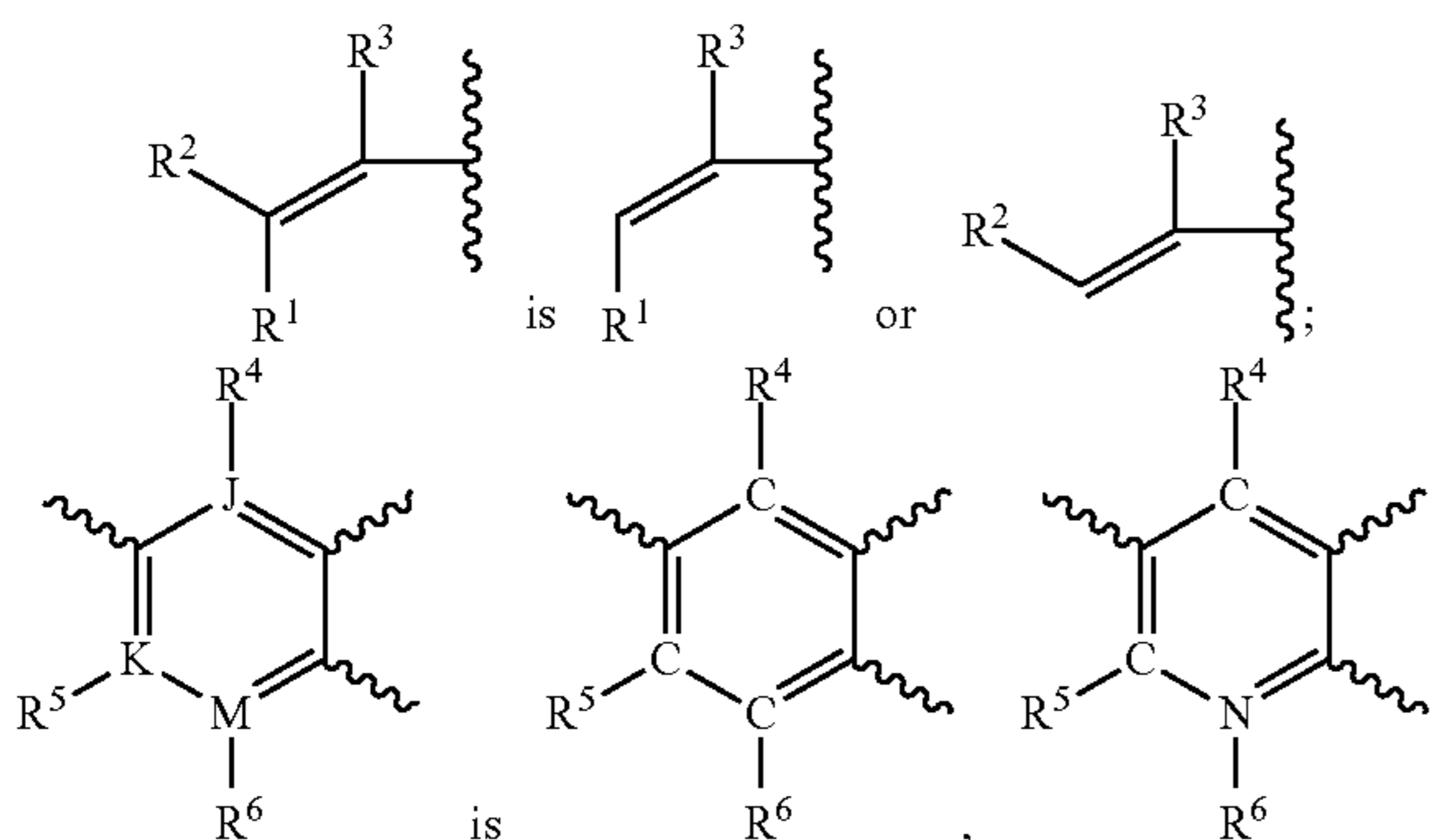
R⁷ and R⁸ are the same or different and selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ heterocycloalkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, halo C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkenyl, halo C₂-C₆ alkenyl, C₂-C₆ alkynyl, halo C₂-C₆ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₆ alkyl, heteroaryl C₁-C₆ alkyl;

R⁹ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ heterocycloalkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy, halo C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, halo C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkenyl, halo C₂-C₆ alkenyl, C₂-C₆ alkynyl, halo C₂-C₆ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl;

R¹⁰ is selected from the group consisting of C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo C₁-C₆ alkyl, halo C₃-C₆ cycloalkyl, unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₆ alkyl, heteroaryl C₁-C₆ alkyl;

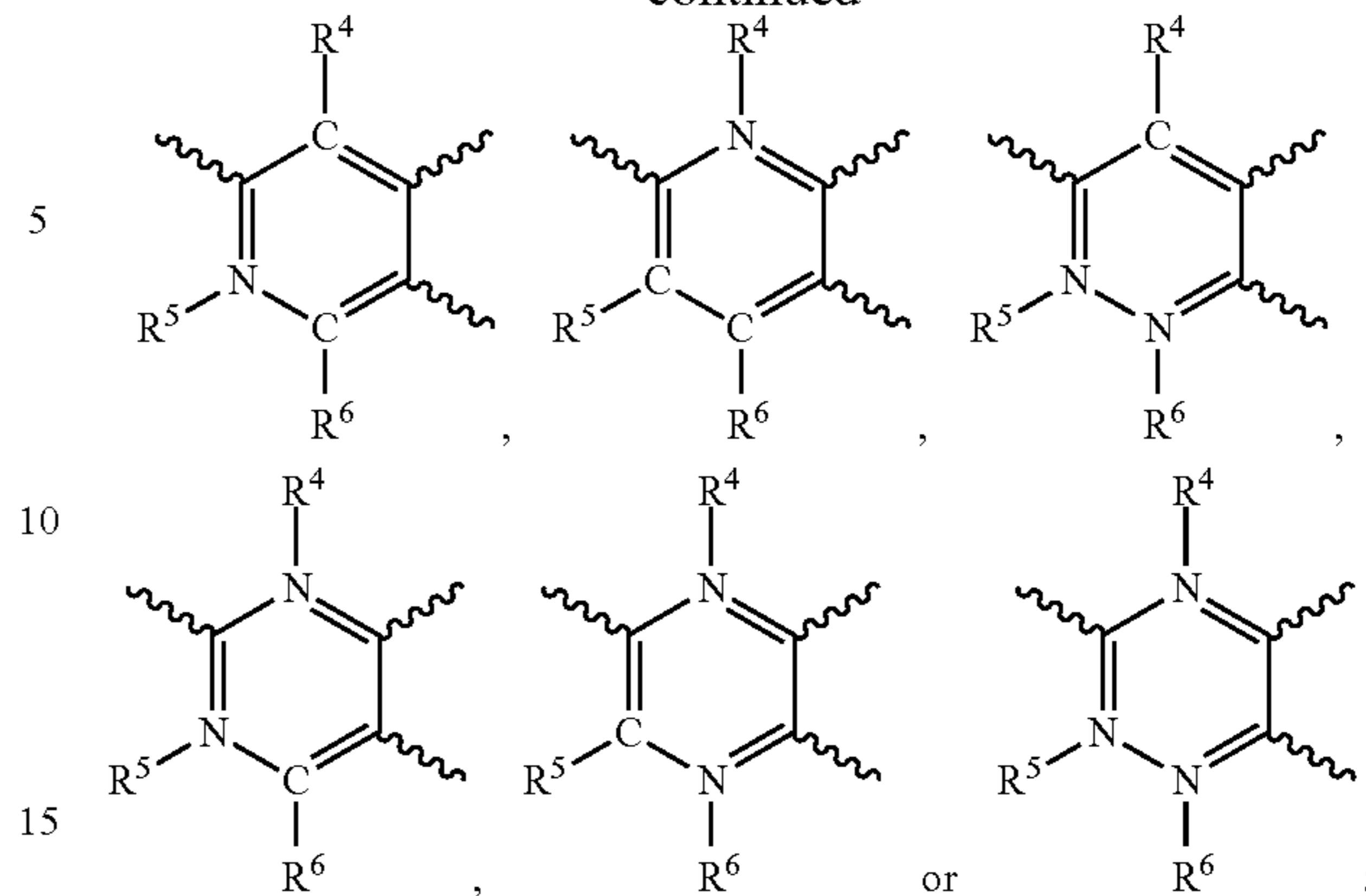
R¹¹ is selected from the group consisting of H, halogen, nitro, cyano, C₁-C₆ alkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy, halo C₁-C₆ alkoxy, C₁-C₆ alkylthiol, C₁-C₆ alkylcarbonyl, C₁-C₆ alkoxy carbonyl, C₂-C₆ alkenyl, halo C₂-C₆ alkenyl, C₃-C₆ alkenyloxy, halo C₃-C₆ alkenyloxy, C₂-C₆ alkynyl, halo C₂-C₆ alkynyl, C₃-C₆ alkynyloxy, halo C₃-C₆ alkynyloxy, halo C₁-C₆ alkylthiol, halo C₁-C₆ alkylcarbonyl, C₁-C₆ alkylamino, halo C₁-C₆ alkylamino, C₂-C₆ dialkylamino, C₁-C₆ alkylcarbonylamino, halo C₁-C₆ alkylcarbonylamino, C₁-C₆ alkylaminocarbonyl or halo C₁-C₆ alkylaminocarbonyl.

The compound of the formula I, a stereoisomer, a cis-trans isomer, a tautomer thereof and a pharmaceutically acceptable salt thereof, further preferred compounds of the formula:



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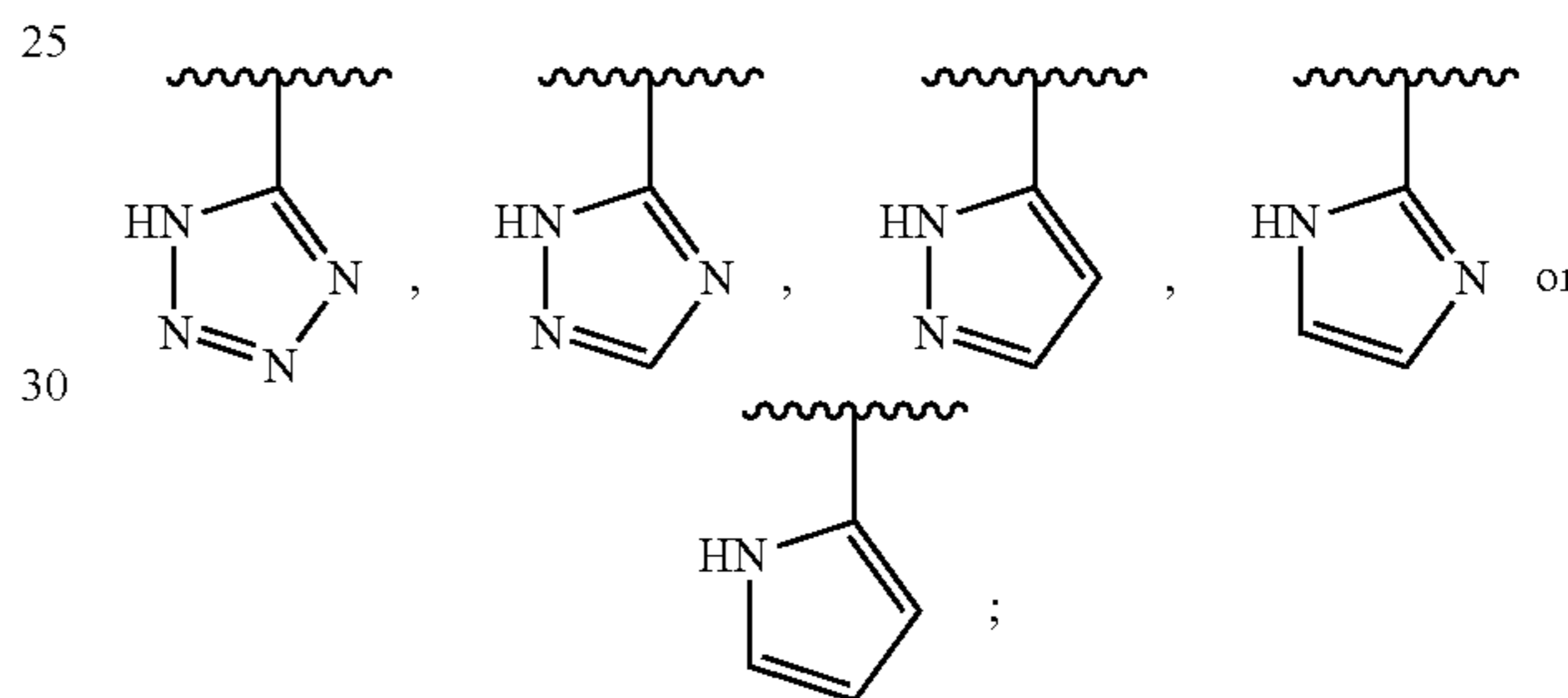


W is selected from NH;

X is selected from CH₂, O or NH;

Y is selected from O or S;

R¹ and R² are selected from COOH, CONHR¹⁰, —CONHSO₂R¹⁰, COOR¹⁰,



R³ is selected from the group consisting of H, C₁-C₂ alkyl, halo C₁-C₂ alkyl, C₂-C₄ alkenyl, halo C₂-C₄ alkenyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: phenyl, pyridyl;

R⁴ is selected from H or halogen;

R⁵ is selected from H or halogen;

R⁶ is selected from the group consisting of H, halogen, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ heterocycloalkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ Alkenyl, C₃-C₆ cycloalkenyl, C₂-C₆ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₆ alkyl, heteroaryl C₁-C₃ alkyl, aryl C₁-C₃ alkoxy, heteroaryl C₁-C₃ alkoxy, aryloxy or heteroaryloxy;

R⁷ and R⁸ are the same or different and selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ heterocycloalkyl, C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkenyl, C₂-C₆ alkynyl, the following groups which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₃: alkyl, heteroaryl C₁-C₃ alkyl;

R⁹ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃-C₆ heterocycloalkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy, halo C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, halo C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkenyl, halo C₂-C₆ alkenyl, C₂-C₆ alkynyl, halo C₂-C₆ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₃ alkyl, heteroaryl C₁-C₃ alkyl;

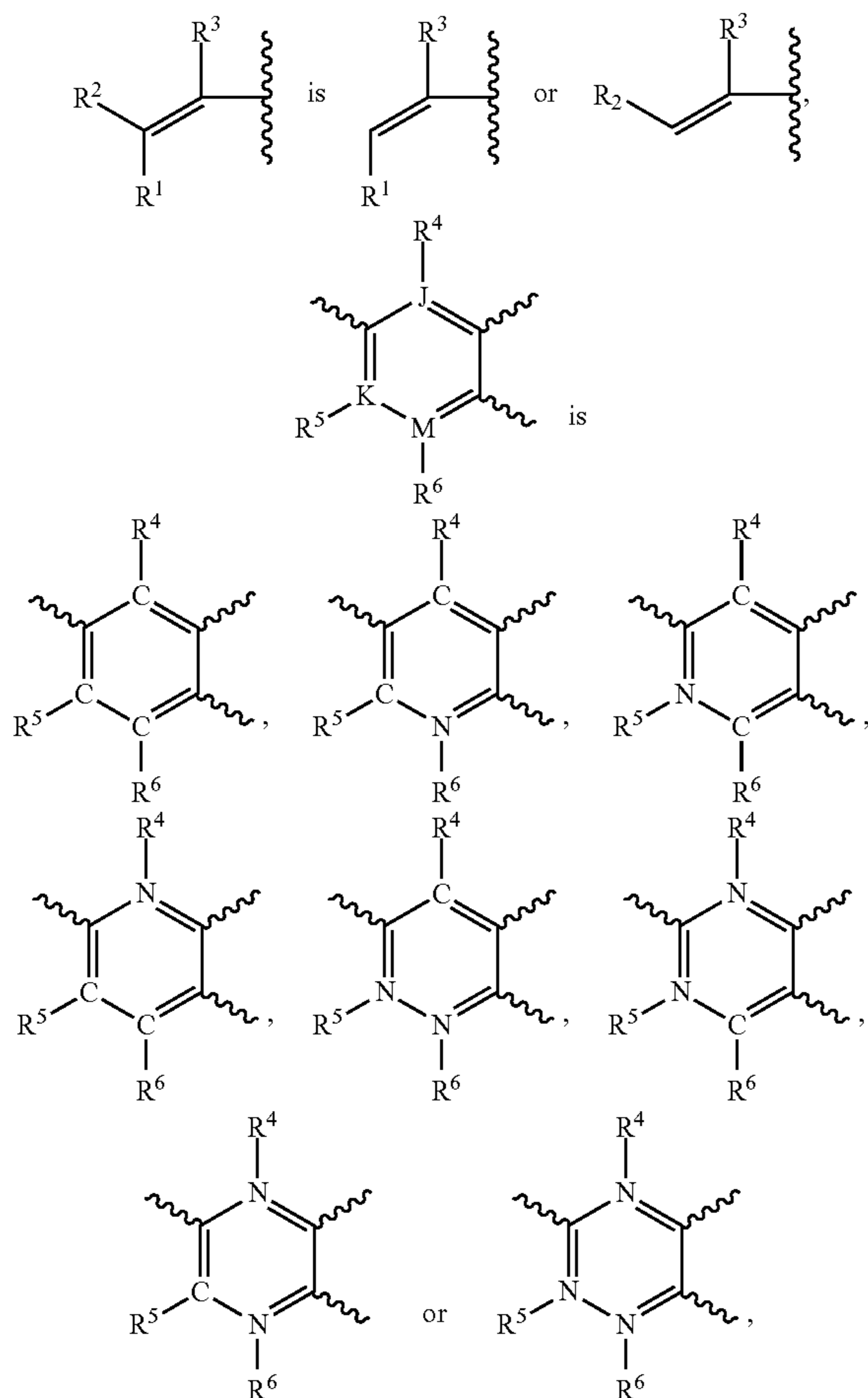
R¹⁰ is selected from the group consisting of C₁-C₃ alkyl, C₃-C₆ cycloalkyl, halo C₁-C₃ alkyl, halo C₃-C₆ cycloalkyl,

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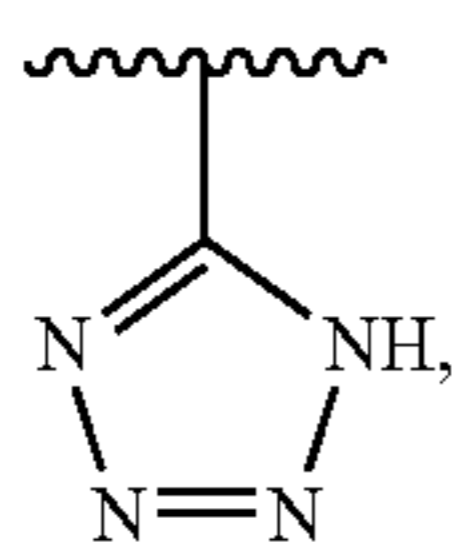
the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₃ alkyl, heteroaryl C₁-C₃ alkyl;

R¹¹ is selected from the group consisting of H, halogen, nitro, cyano, C₁-C₆ alkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy, halo C₁-C₆ alkoxy, C₁-C₆ alkylthiol, C₁-C₆ alkylcarbonyl, C₁-C₆ alkoxy carbonyl, C₂-C₆ alkenyl, halo C₂-C₆ alkenyl, C₃-C₆ alkenyloxy, halo C₃-C₆ alkenyloxy, C₂-C₆ alkynyl, halo C₂-C₆ alkynyl, C₃-C₆ alkynyloxy, halo C₃-C₆ alkynyloxy, halo C₁-C₆ alkylthiol, halo C₁-C₆ alkylcarbonyl, C₁-C₆ alkylamino, halo C₁-C₆ alkylamino, C₂-C₆ dialkylamino, C₁-C₆ alkylcarbonylamino, halo C₁-C₆ alkylcarbonylamino, C₁-C₆ alkylaminocarbonyl or halo C₁-C₆ alkylaminocarbonyl.

The compound of the formula I, a stereoisomer, a cis-trans isomer, a tautomer thereof and a pharmaceutically acceptable salt thereof, wherein a further preferred compound is:



W is selected from NH;
X is selected from CH₂, O or NH;
Y is selected from O or S;
R¹ and R² are selected from COOH,



CONHSO₂CH₃, CONHSO₂CF₃ or COOCH₂CH₃;

6

R³ is selected from H, CH₃, CH₂CH₃ or CF₃;

R⁴ is selected from H;

R⁵ is selected from H;

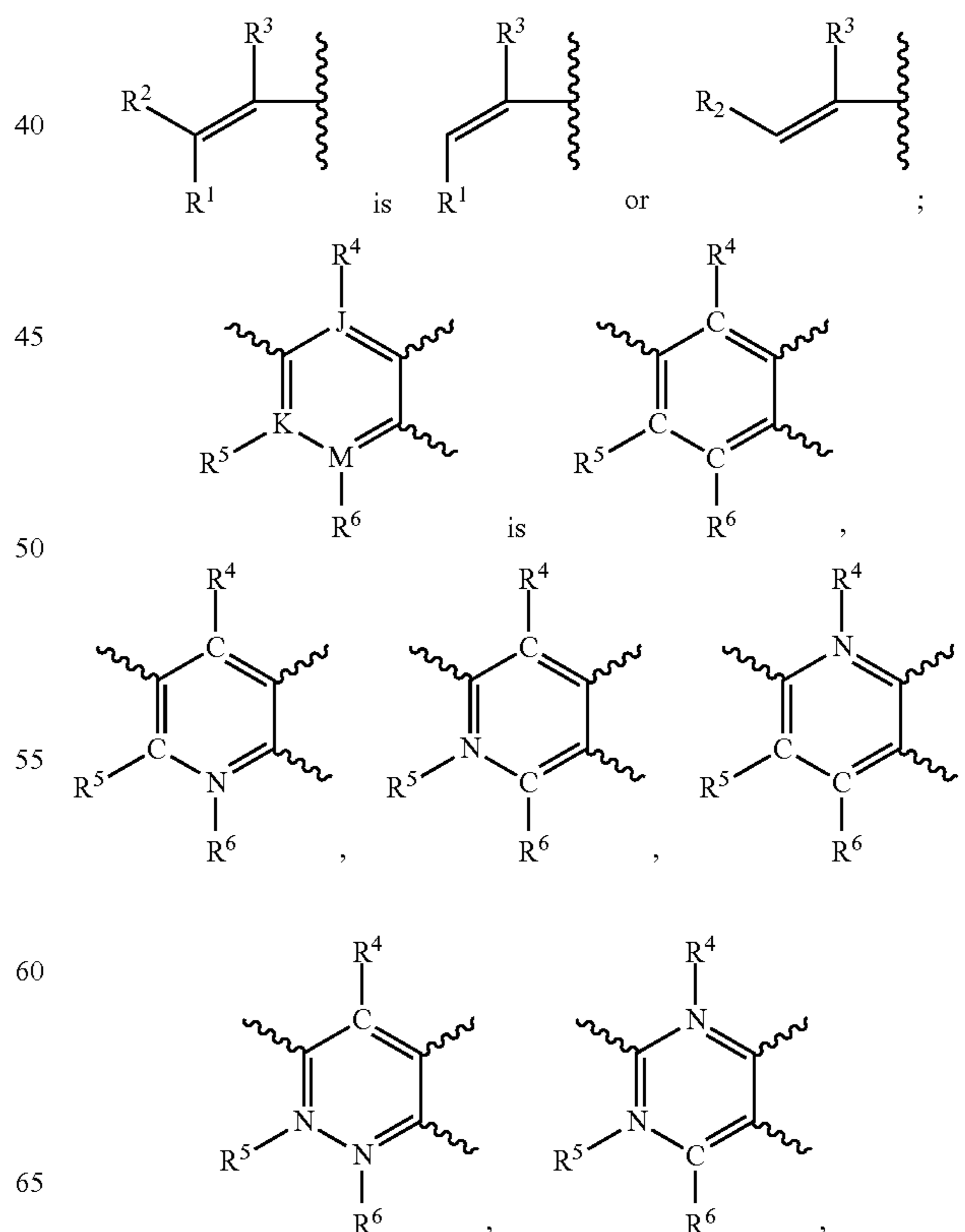
R⁶ is selected from H;

R⁷ and R⁸ are the same or different and selected from the group consisting of H, methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl;

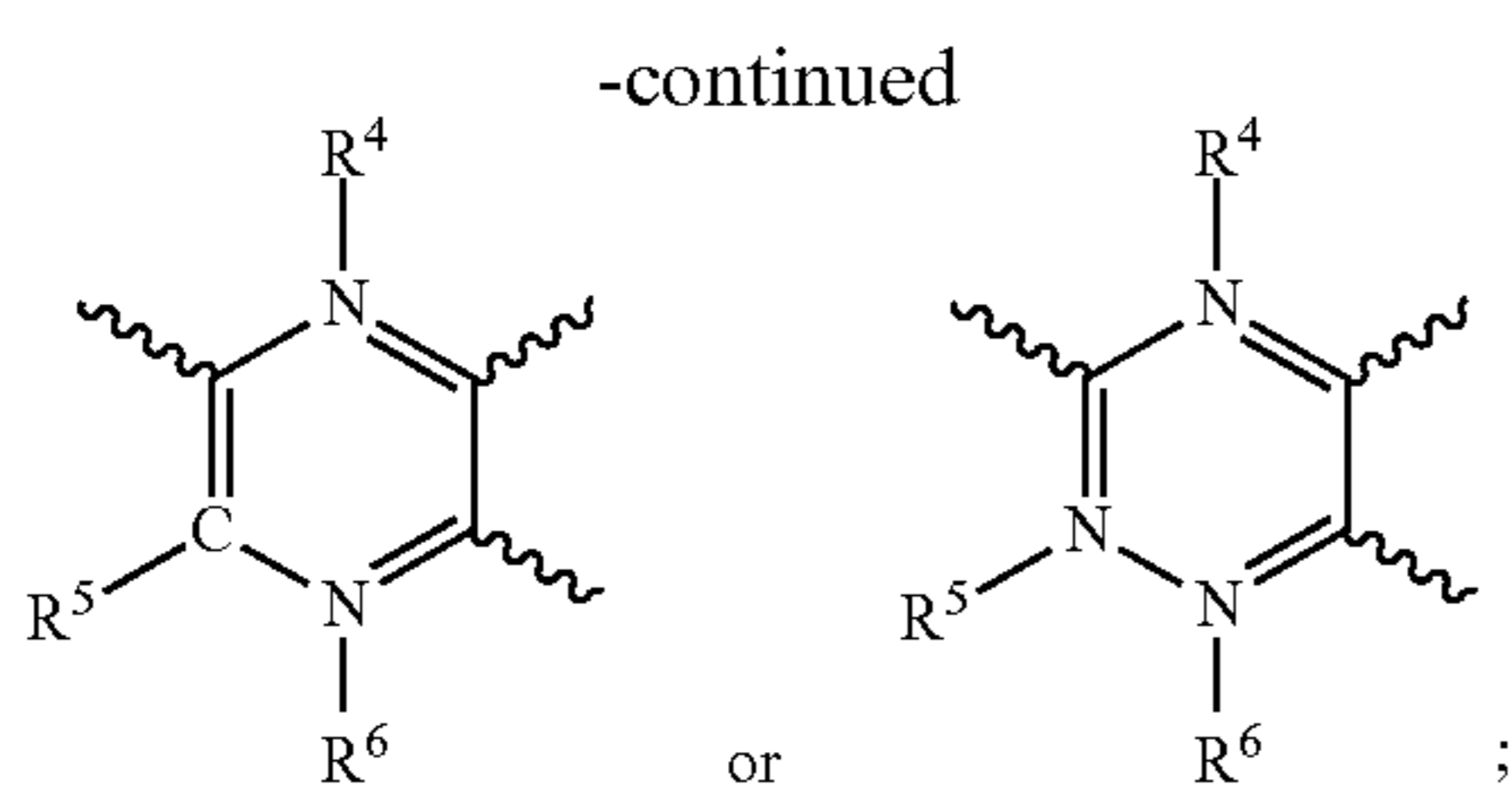
R⁹ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₃₋₆ heterocycloalkyl, halo C₁-C₆ alkyl, C₁-C₆ alkoxy, halo C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, halo C₁-C₆ alkoxy C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkenyl, halo C₂-C₆ alkenyl, C₂-C₆ alkynyl, halo C₁-C₆ alkynyl, the following group which is unsubstituted or substituted by 1-5 R¹¹: aryl, heteroaryl, aryl C₁-C₃ alkyl, heteroaryl C₁-C₃ alkyl;

R¹¹ is selected from the group consisting of H, halogen, nitro, cyano, C₁-C₃ alkyl, halo C₁-C₃ alkyl, C₁-C₃ alkoxy, halo C₁-C₃ alkoxy, C₁-C₃ alkylthiol, C₁-C₃ alkylcarbonyl, C₁-C₃ alkoxy carbonyl, C₂-C₃ alkenyl, halo C₂-C₃ alkenyl, C₃-C₆ alkenyloxy, halo C₃-C₆ alkenyloxy, C₂-C₃ alkynyl, halo C₂-C₃ alkynyl, C₃-C₆ alkynyloxy, halo C₃-C₆ alkynyloxy, halo C₁-C₃ alkylthiol, halo C₁-C₃ alkylcarbonyl, C₁-C₃ alkylamino, halo C₁-C₃ alkylamino, C₂-C₃ dialkylamino, C₁-C₃ alkylcarbonylamino, halo C₁-C₃ alkylcarbonylamino, C₁-C₃ alkylaminocarbonyl or halo C₁-C₃ alkylaminocarbonyl.

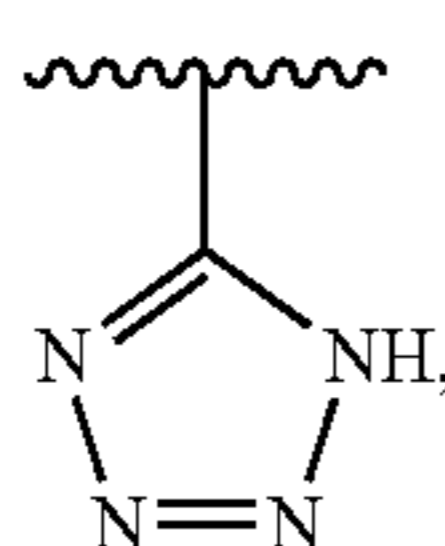
The compound of the formula I, a stereoisomer, a cis-trans isomer, a tautomer thereof and a pharmaceutically acceptable salt thereof, and a still further preferred compound of the formula:



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W is selected from NH;
 X is selected from CH₂, O or NH;
 Y is selected from O or S;
 R¹ and R² are selected from COOH,



CONHSO₂CH₃, CONHSO₂CF₃ or COOCH₂CH₃;

R³ is selected from H, CH₃, CH₂CH₃ or CF₃;

R⁴ is selected from H;

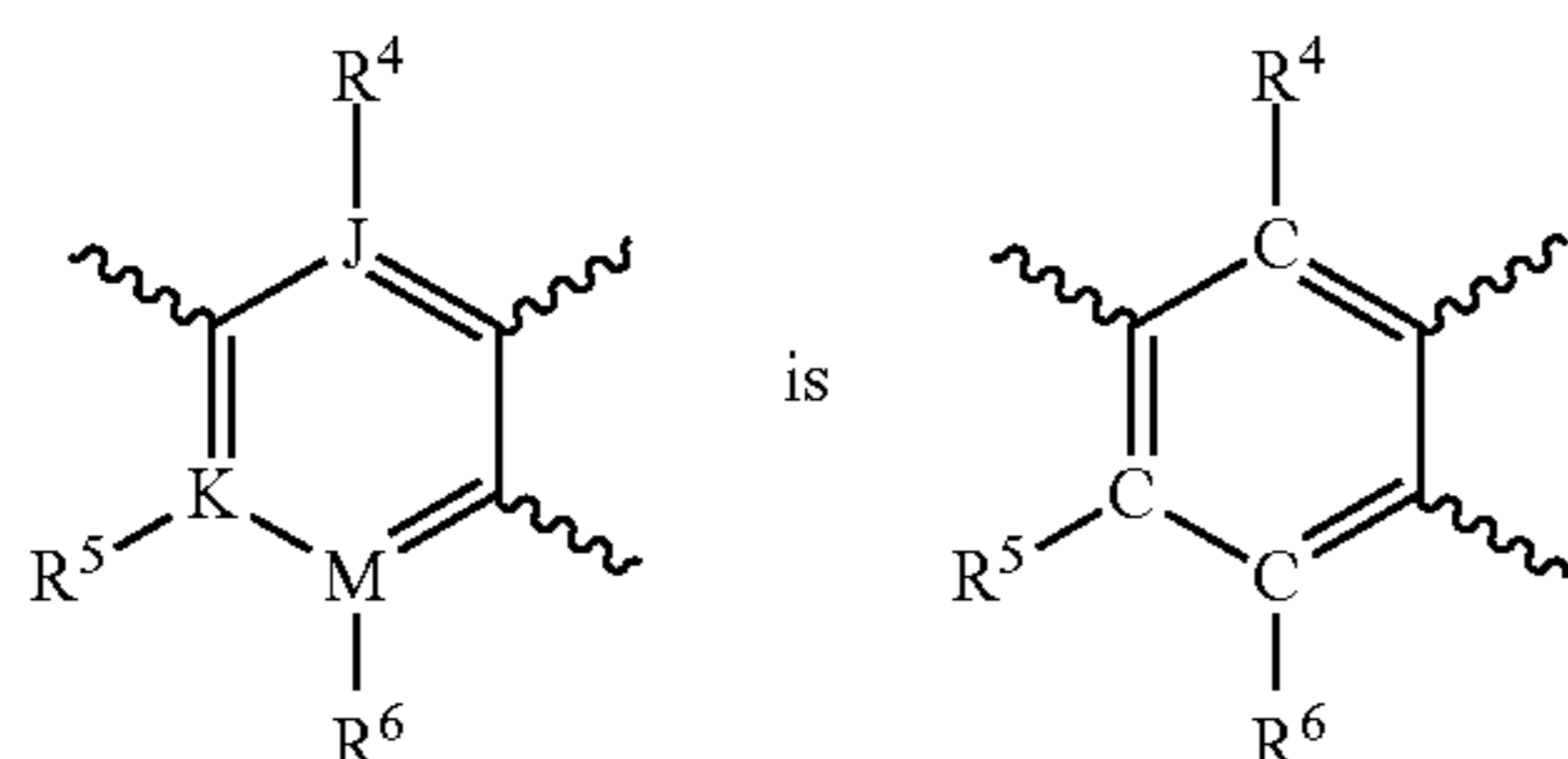
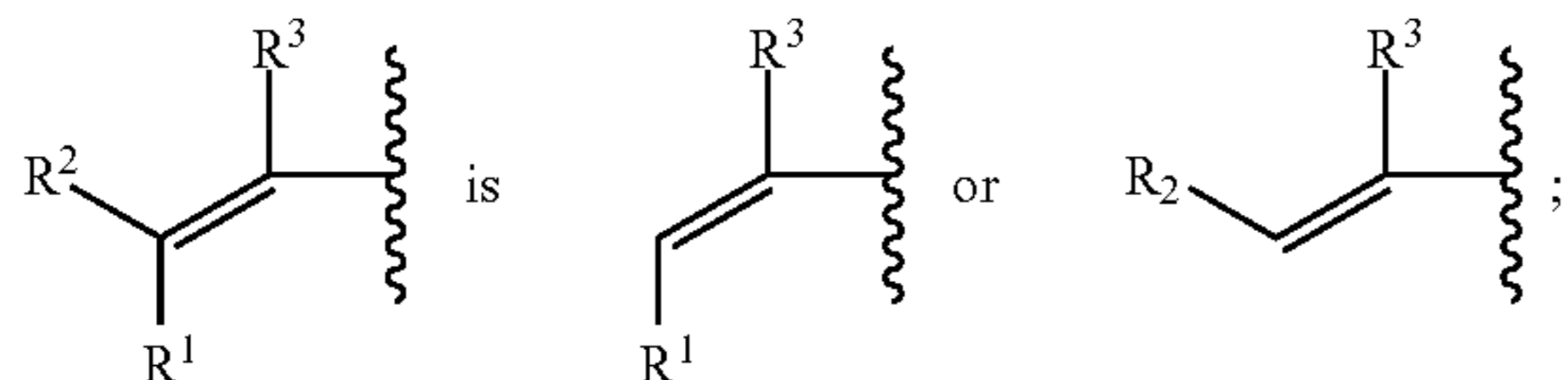
R⁵ is selected from H;

R⁶ is selected from H;

R⁷ and R⁶ are the same or different and selected from the group consisting of H, methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl;

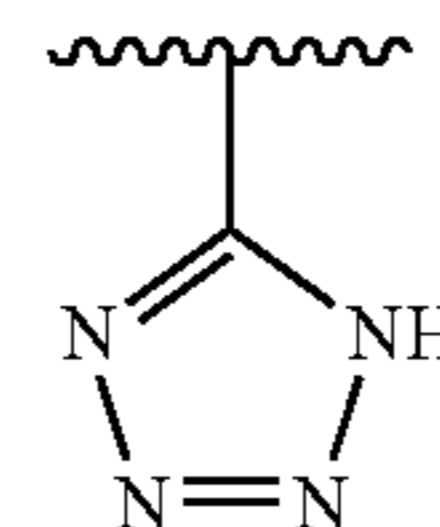
R⁹ is selected from the group consisting of phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2,4-dimethylphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,4-difluorophenyl, 2-fluoro-4-methylphenyl, 3-trifluoromethyl-4-chlorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,4-dichlorophenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 5-methylisoxazolyl.

The compound of the formula I, a stereoisomer, a cis-trans isomer, a tautomer thereof and a pharmaceutically acceptable salt thereof, and a still further preferred compound of the formula:



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W is NH;
 X is NH or CH₂;
 Y is O;
 R¹ and R² is selected from COOH,



or COOCH₂CH₃;

R³ is selected from CH₃;

R⁴ is selected from H;

R⁵ is selected from H;

R⁶ is selected from H;

R⁷ and R⁸ are the same or different and selected from n-butyl or isobutyl;

R⁹ is selected from the group consisting of 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2,4-dimethylphenyl, 2,4-difluorophenyl, 2-fluoro-4-methylphenyl, 3-trifluoromethyl-4-chlorophenyl, phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,4-dichlorophenyl, 2-fluorophenyl, 4-fluorophenyl, 3-fluorophenyl or 5-methylisoxazolyl.

The above pharmaceutically acceptable salt prepared by compound and base can be sodium salt, potassium salt, calcium salt, zinc salt, magnesium salt and other metal ion salt. It also can be meglumine salt, aminobutanediol salt, aminoethanol salt, lysine salt, arginine salt and other organic salt. Acid radical salt can be hydrochloride, sulfate, hydrobromate, mesylate, citrate, oxalate, succinate, maleate, citrate, acetate, lactate, phosphate, hydroiodate, nitrate, tartaric acid, p-toluene sulfonic acid, etc.

In the definition of compound of formula I, the terms are generally defined as follows:

Halogen: fluorine, chlorine, bromine or iodine.

Alkyl: straight or branched alkyl, such as methyl, ethyl, propyl, isopropyl, n-butyl, or tert-butyl.

Cycloalkyl: a heterocyclic ring alkyl; such as cyclopropyl, cyclopentyl, or cyclohexyl, which is substituted or unsubstituted. Substituent group such as methyl, halogen, etc.

Heterocyclic alkyl: a ring alkyl substituted or unsubstituted containing one or more N, O, S heteroatoms, such as tetrahydrofuranyl or cyclopentanyl. Substituent group such as methyl, halogen, etc.

Halo alkyl: straight or branched alkyl, in which the hydrogen atoms may be partially or completely replaced by halo atoms, such as chloromethyl, dichloromethyl, trichloromethyl, fluoromethyl, difluoromethyl, trifluoromethyl, etc.

Alkoxy: Straight or branched alkyl groups are linked to the structure by oxygen atom bonds.

Halo alkoxy: Straight or branched alkoxy groups in which the hydrogen atoms may be partially or completely replaced by halogen atoms. For example, chloromethoxy, dichloromethoxy, trichloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, chlorofluoromethoxy, trifluoroethoxy, etc.

Alkoxy alkyl: The alkoxy group is linked to the structure by alkyl group. Such as, —CH₂OCH₃, —CH₂OCH₂CH₃.

Halo alkoxy alkyl: The hydrogen atoms in alkoxyalkyl groups may be partially or completely replaced by halogen atoms. Such as, —CH₂OCH₂CH₂Cl.

Alkylthiol: Straight or branched alkyl groups that is bonded to a structure by an atomic sulfur bond.

Halo alkylthiol: Straight or branched alkylthiol groups in which the hydrogen atoms may be partially or completely replaced by halogen atoms. For example, chloromethane, dichloromethane, trichloromethane, fluoromethane, difluoromethane, trifluoromethane, chlorofluoromethane, etc.

Alkylamino: Straight or branched alkyl groups bonded to a structure by a nitrogen atom.

Halo alkylamino: Straight or branched alkylamino groups in which the hydrogen atoms may be partially or completely replaced by the halogen atoms.

Alkenyl: Straight or branched alkenes groups, such as vinyl, 1-propylene, 2-propylene, and different butylene, pentenyl, and hexenyl isomers. Alkenes also include polyenes, such as 1,2-propylene, and 2,4-hexadienyl.

Halo alkene: Straight or branched alkenes groups in which hydrogen atoms may be partially or completely replaced by halogen atoms.

Alkynyl: Straight or branched alkynes groups, such as acetylenyl, 1-propargynyl, 2-propargynyl, and different butynyl, pentynyl, and hexynyl isomers. Alkynyl also includes groups consisting of multiple triple bonds, such as 2,5-hexylenyl.

Halo alkynyl: Straight or branched alkynes groups in which hydrogen atoms may be partially or completely replaced by halogen atoms.

Alkenyloxy: Straight or branched alkenyl groups bonded to a structure by an oxygen bond.

Halo alkenyloxy: Straight or branched alkenyl groups in which the hydrogen atoms may be partially or completely replaced by halogen atoms.

Alkynyloxy: Straight or branched alkynyl groups bonded to a structure by an oxygen atom.

Halo alkynyloxy: Straight or branched alkynyl groups in which the hydrogen atoms may be partially or completely replaced by halogen atoms.

Alkyl carbonyl: Straight or branched alkyl groups bonded to a structure by a carbonyl group ($-\text{CO}-$), such as an acetyl group.

Halo alkyl carbonyl: Straight or branched Alkyl carbonyl groups in which the hydrogen atoms may be partially or completely replaced by halogen atoms.

Alkoxy carbonyl: Straight or branched alkoxy groups bonded to a structure by a carbonyl group ($-\text{CO}-$). Such as $-\text{COOCH}_3$, $-\text{COOCH}_2\text{CH}_3$.

Halo alkoxy carbonyl: Straight or branched alkoxy carbonyl groups in which the hydrogen atoms may be partially or completely replaced by halogen atoms. Such as $-\text{COOCH}_2\text{CF}_3$, $-\text{COOCH}_2\text{CH}_2\text{Cl}$ etc.

Alkyl carbonyl amino: Such as $-\text{NHCOCH}_3$, $-\text{NHCOC}(\text{CH}_3)_3$

Alkyl aminocarbonyl: Such as $-\text{C}(=\text{O})\text{NHCH}_3$, $-\text{C}(=\text{O})\text{N}(\text{CH}_3)_2$

The aromatic parts of aryl, aryl alkyl, aryloxy, aryl aryloxy and aryl amino include phenyl or naphthalene group, etc.

Hetero aryl groups are five-membered rings or six-membered rings containing one or more N, O, S hetero atoms. For example, furanyl, pyrazolyl, thiazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, quinolyl, etc.

Heteroaryl part of heteroaryl alkyl, heteroaryloxy and heteroaryl alkoxy groups refers to a five or a six-membered ring containing one or more N, O, S heteroatoms. For example, furyl, pyrazolyl, thiazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, quinolyl, benzoxazolyl, indolyl, etc.

The application of a vinylarene derivative, the compound shown in formula I, its stereoisomer, cis-trans isomer, tau-

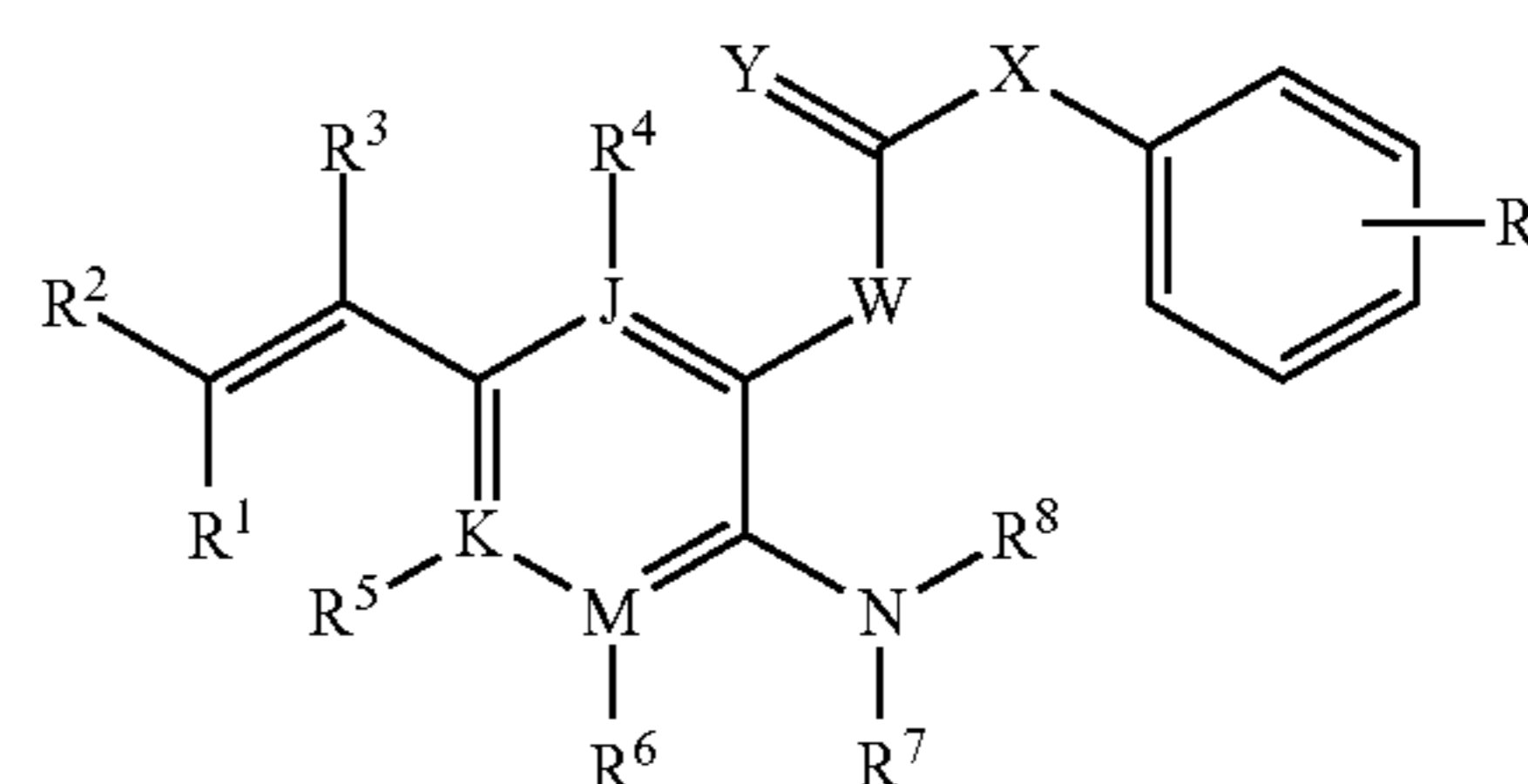
tomers and pharmaceutically acceptable salt thereof, or a combination thereof, in the preparation of an inhibitor for inhibiting the activity of IDO-1 enzyme.

The application of a vinylarene derivative, the compound shown in formula I, its stereoisomer, cis-trans isomer, tautomer and pharmaceutically acceptable salt thereof, or a combination thereof, in the preparation of an anti-cancer drug, a viral infectious agent, a depressant, an organ transplant rejection agent or an autoimmune enhancer.

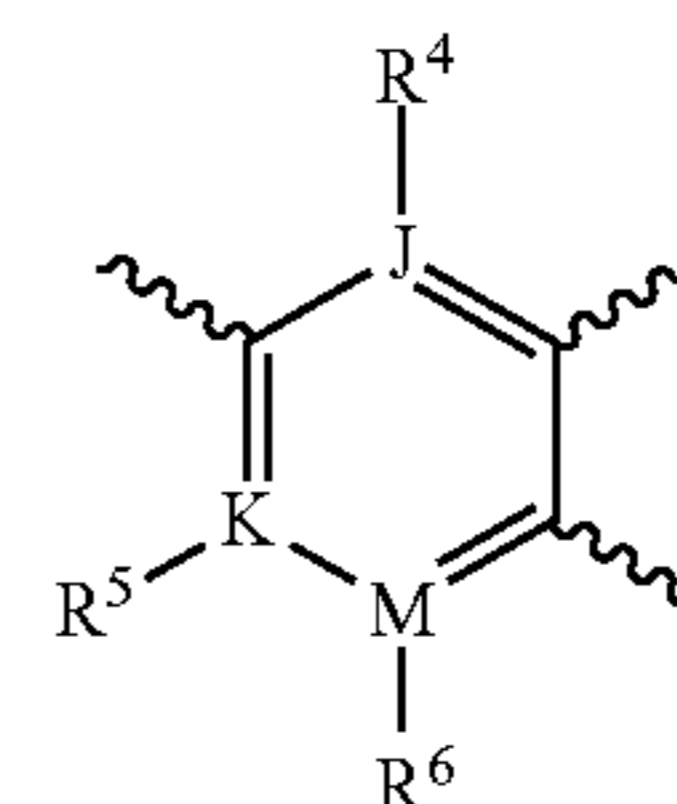
The cancer is colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, cervical cancer, kidney cancer, head and neck cancer, lymphoma, leukemia or melanoma.

A pharmaceutical composition comprising any one or more compounds shown in formula I, its stereoisomer, cis-trans isomer, tautomer, pharmaceutically acceptable salt thereof and pharmaceutically acceptable carriers or diluents.

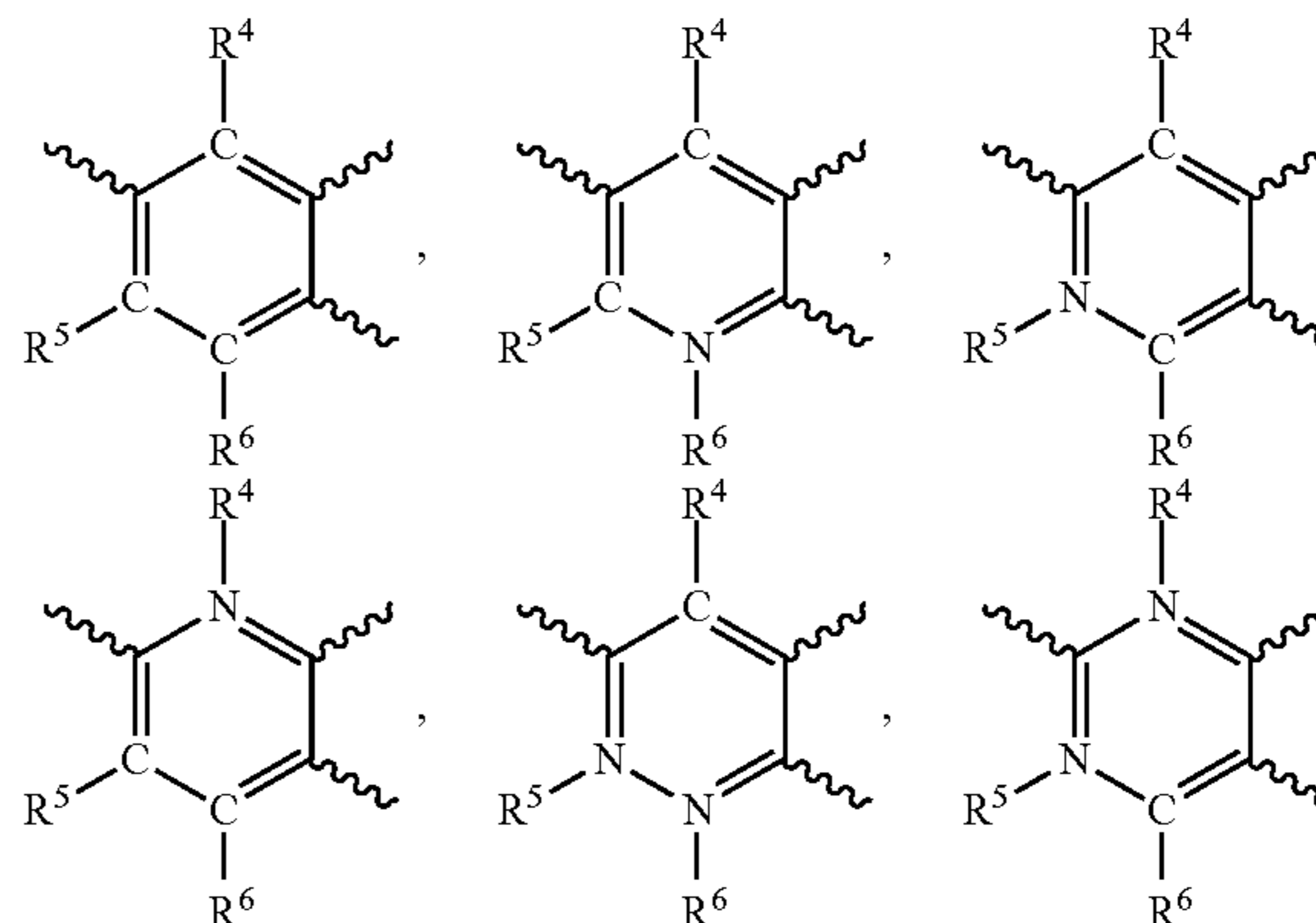
The compounds in the present invention, stereoisomer can be formed by connecting different substituents with carbon-carbon double bond (Z and E are used to represent different configurations, respectively). The present invention includes Z-type isomer and E-type isomer and their mixtures in any proportion.



In formula I

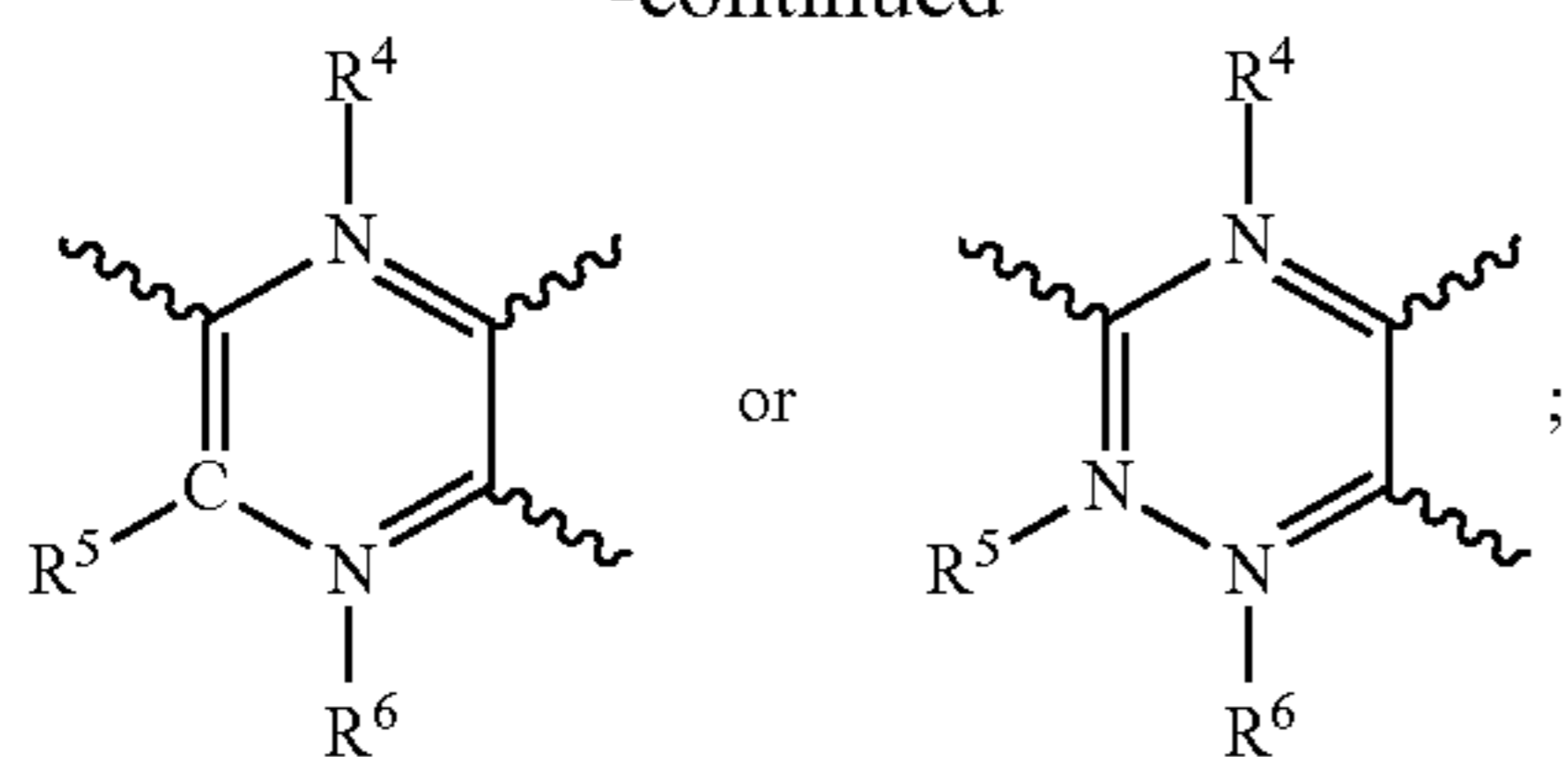


the specific substituent is:



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-continued



In formula I, the specific substituent of W is CH₂, O or NH;

In formula I, the specific substituent of X is CH₂, O or NH;

In formula I, the specific substituent of Y is O or S;

In formula I, the specific substituents in R³ are H, CH₃, CH₂CH₃, CH₂CH₂CH₃ and CF₃.

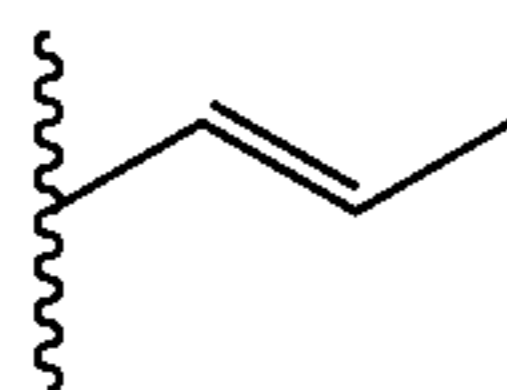
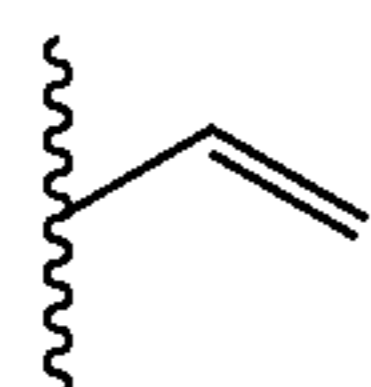
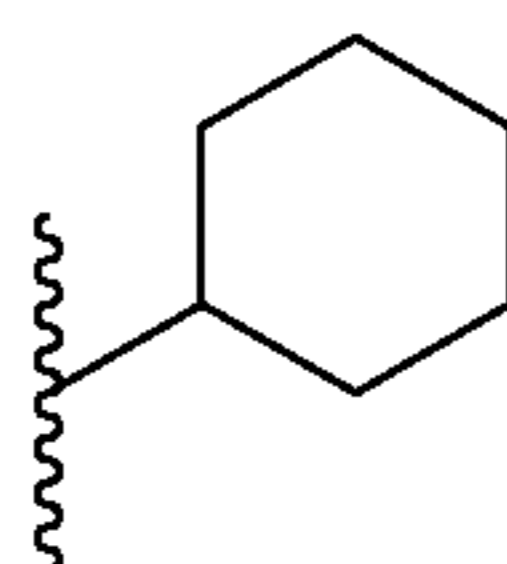
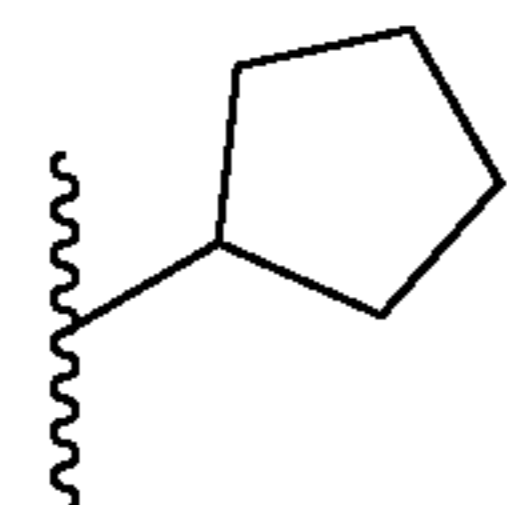
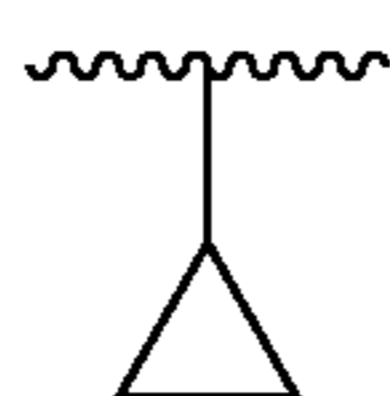
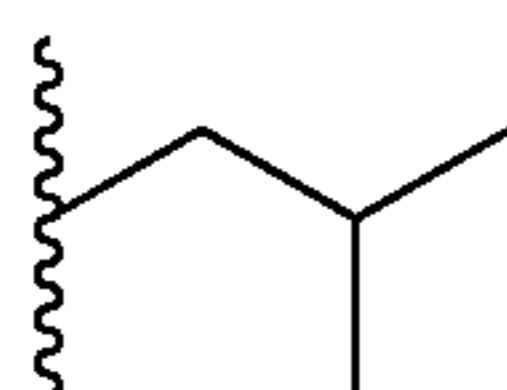
In formula I, the specific substituents of R⁴ are H, Cl, Br and I.

In formula I, the specific substituents of R⁵ are H, Cl, Br and I.

The specific substituents of R⁶ in formula I are shown in table 1,

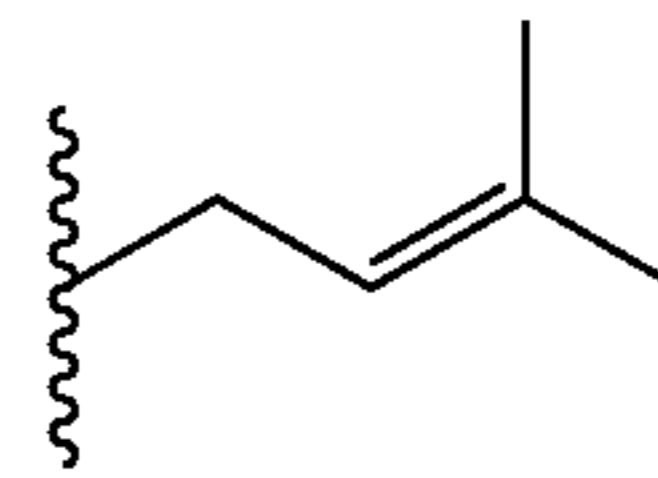
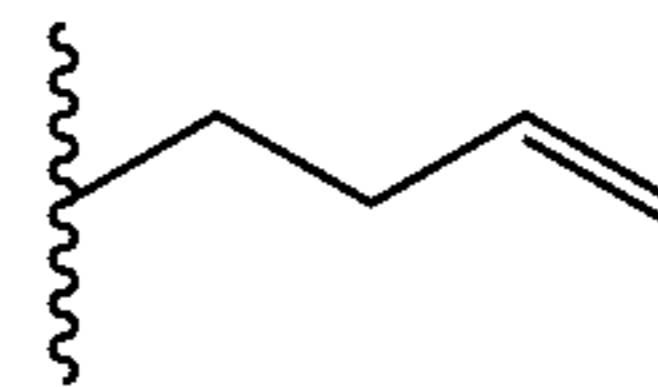
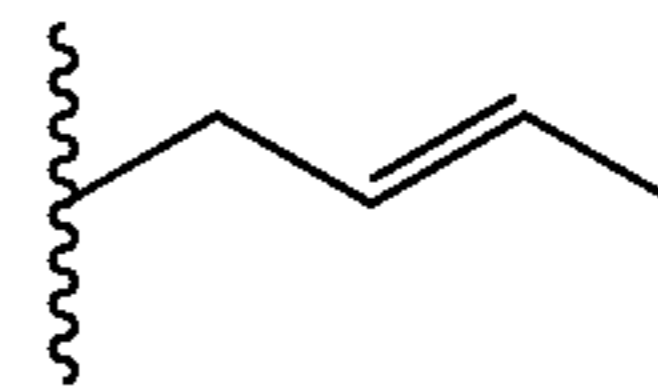
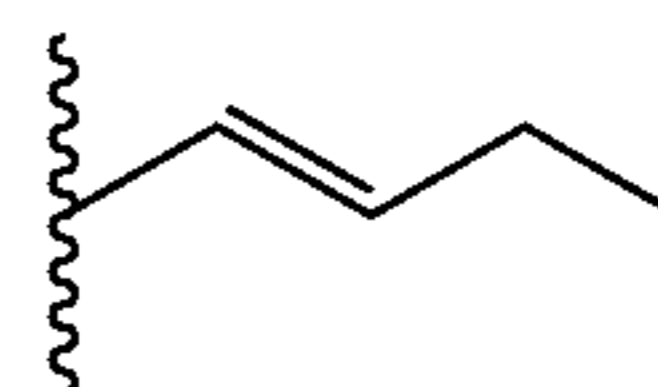
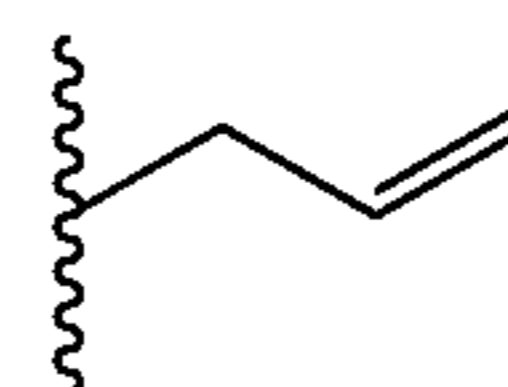
TABLE I

H
Cl
Br
I
NO₂
CN
CH₃
CH₂CH₃
CH₂CH₂CH₃
CH₂CH₂CH₂CH₃
CH₂(CH₂)₃CH₃



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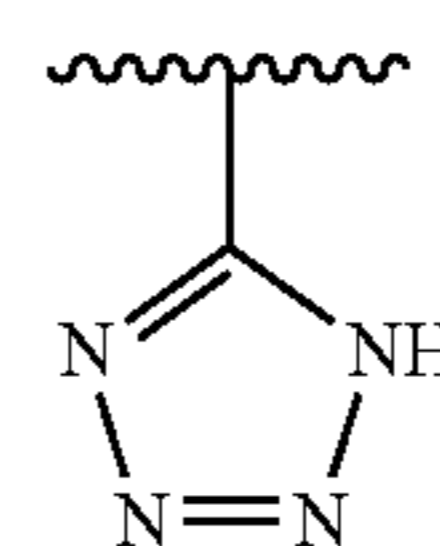
TABLE I-continued



In formula I, R¹ and R² are the same or different, and the specific substituents are shown in table 2. The definitions of other substituents in formula I, such as R³, R⁴ and R⁵, are the same as above.

TABLE 2

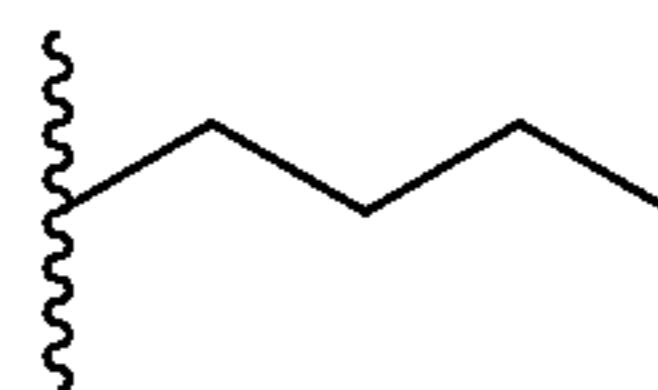
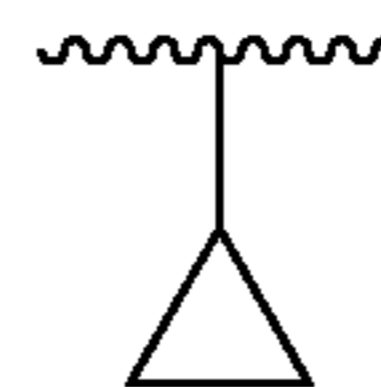
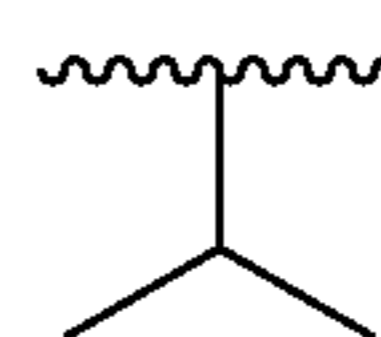
H
COOH
COOCH₂CH₃
CONHSO₂CH₃
CONHSO₂CF₃



In formula I, R⁷ and R⁸ are the same or different, and the specific substituents are shown in table 3. The definitions of other substituents in formula I, such as R³, R⁴ and R⁵, are the same as above.

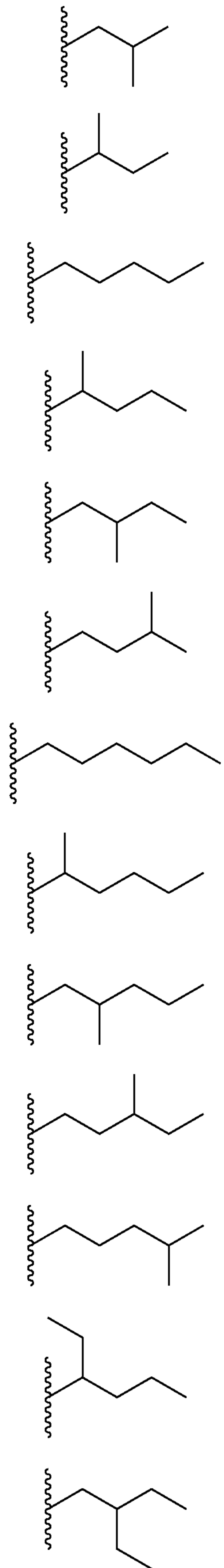
TABLE 3

H
CH₃
CH₂CH₃
CH₂CH₂CH₃



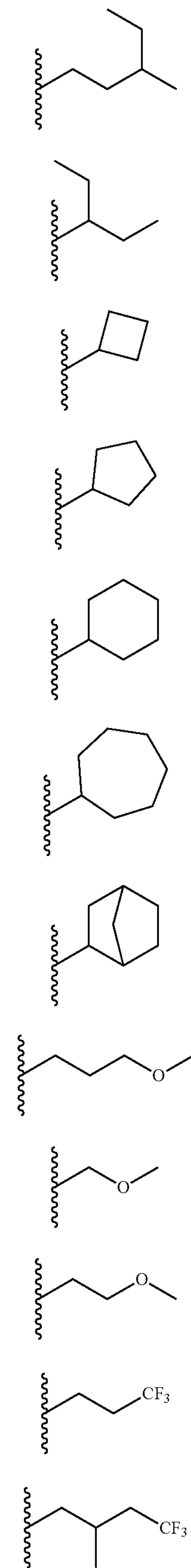
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TABLE 3-continued



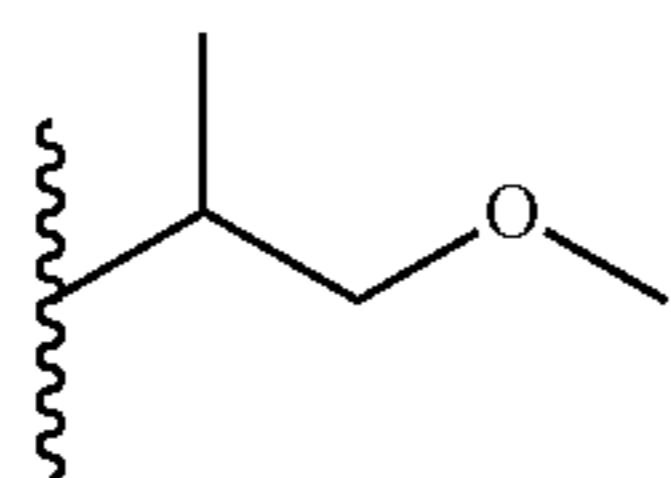
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TABLE 3-continued



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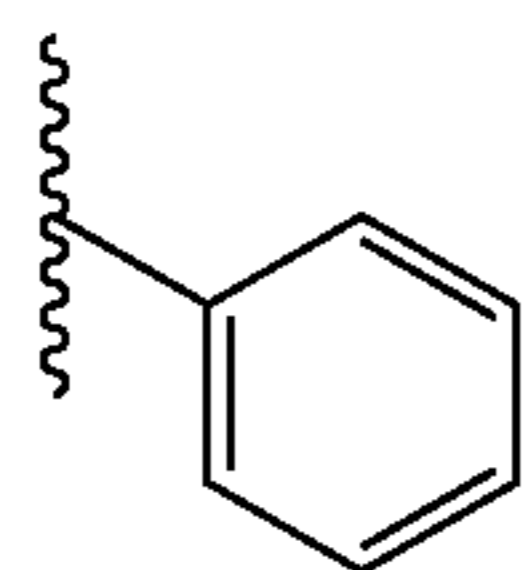
TABLE 3-continued



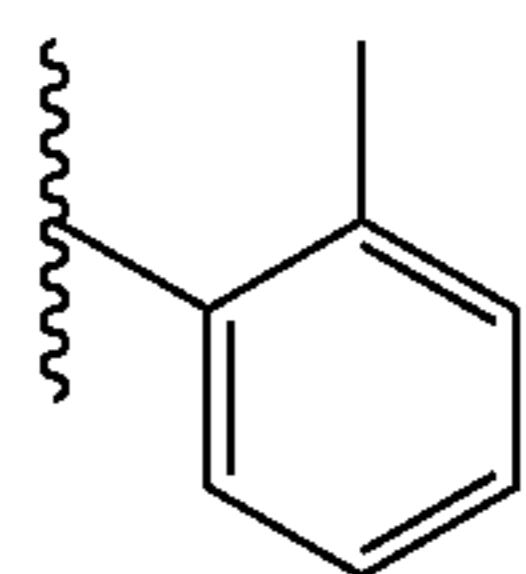
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The specific substituents of R⁹ in formula I, are shown in table 4. The definitions of other substituents in formula I, such as R³, R⁴ and R⁵, are the same as above.

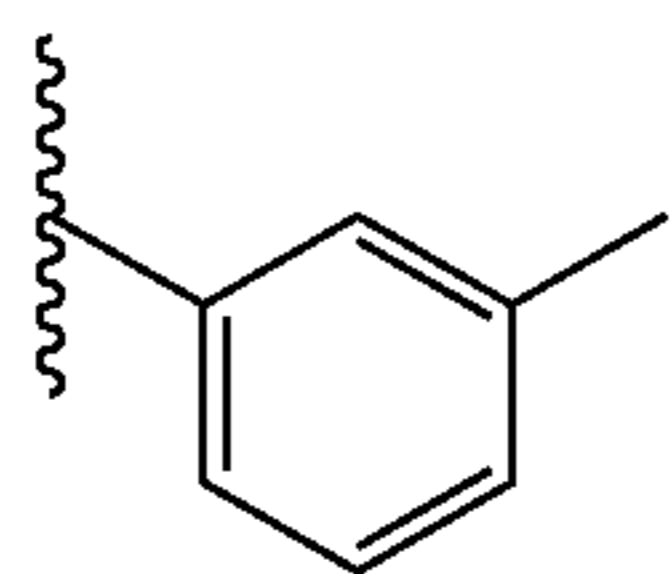
TABLE 4



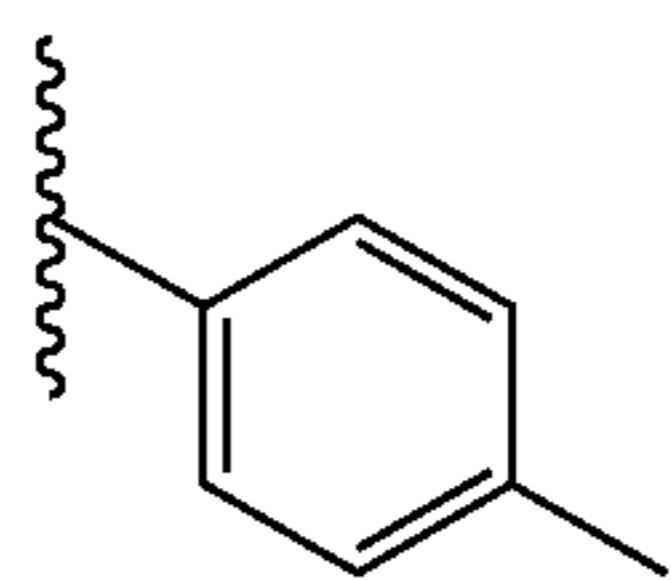
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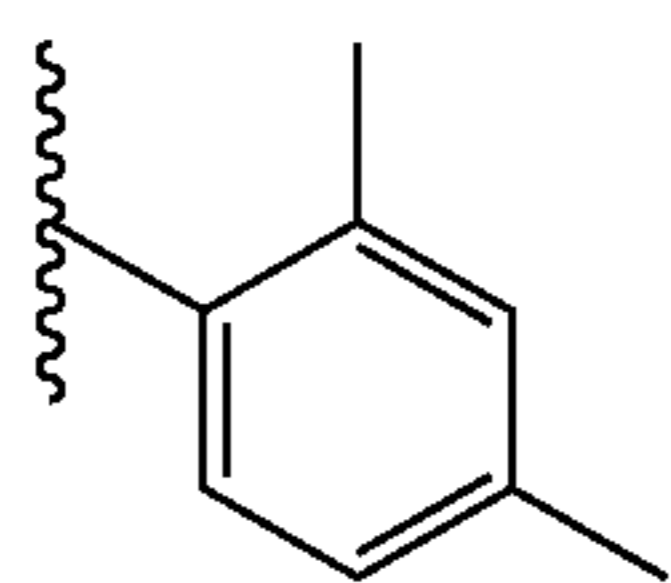
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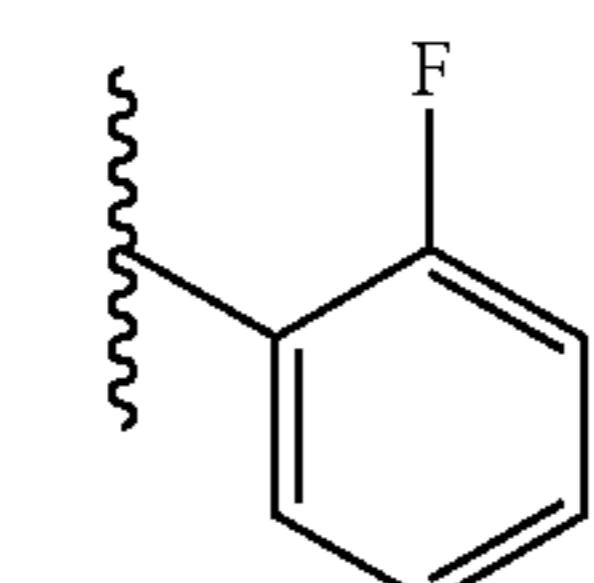
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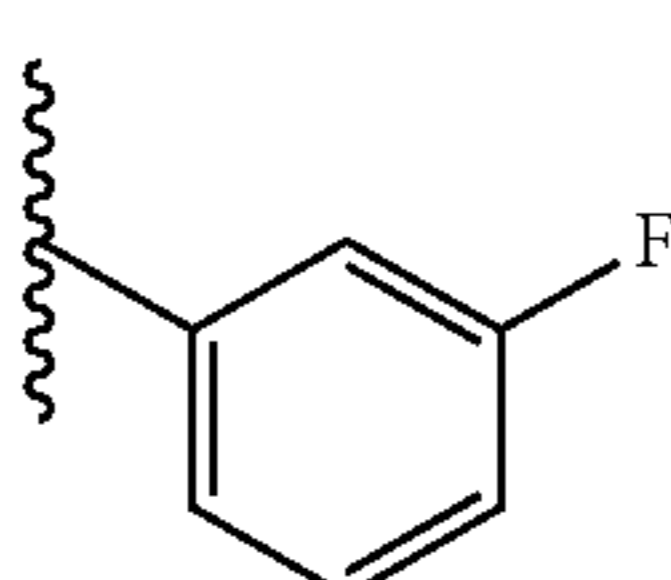
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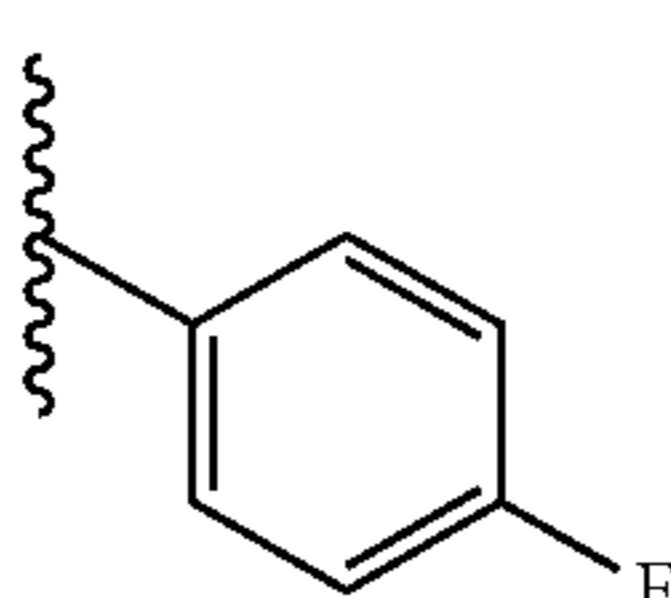
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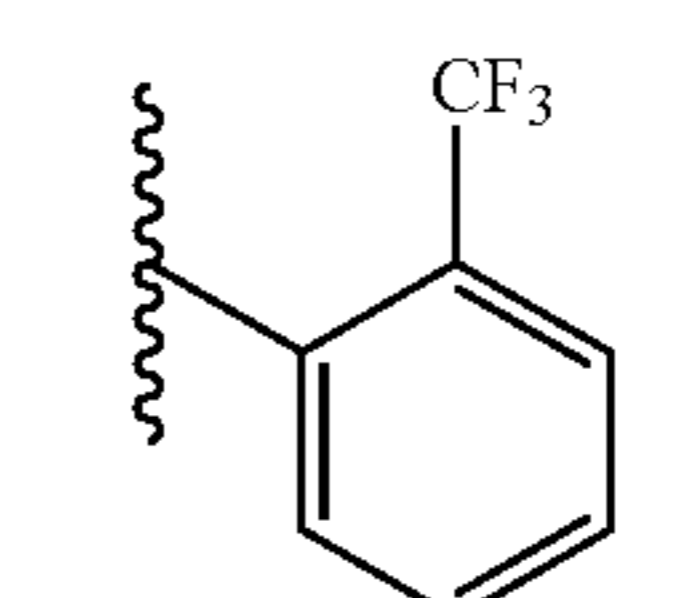
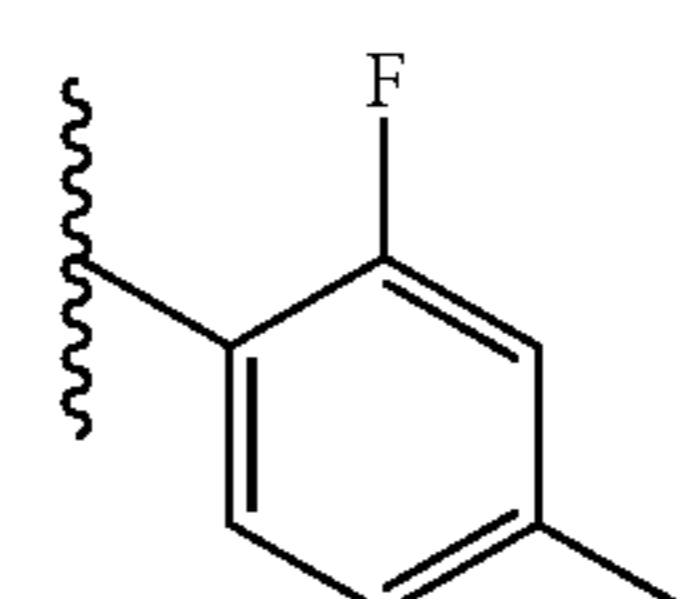
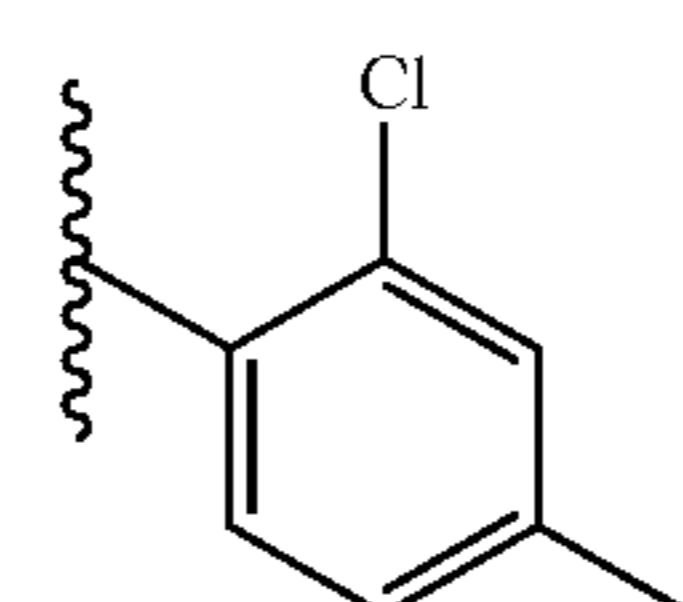
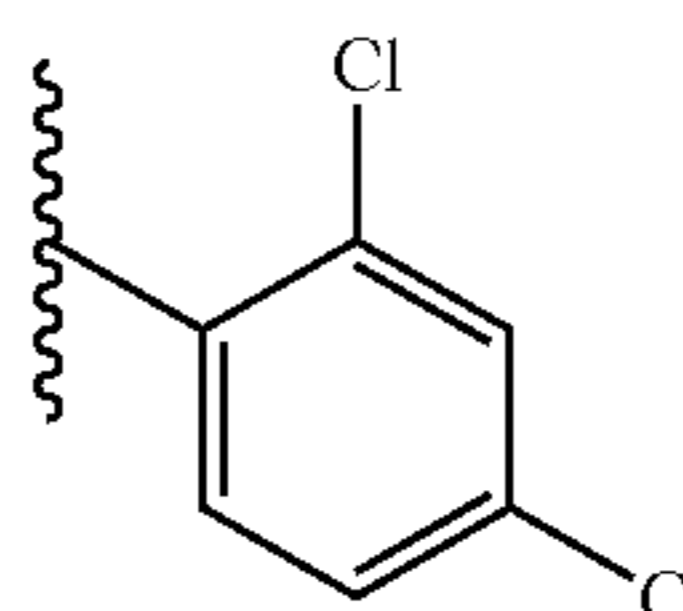
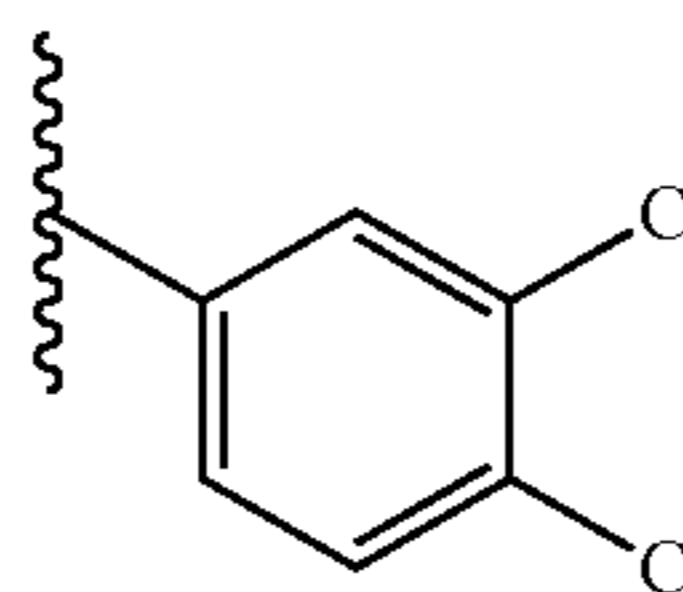
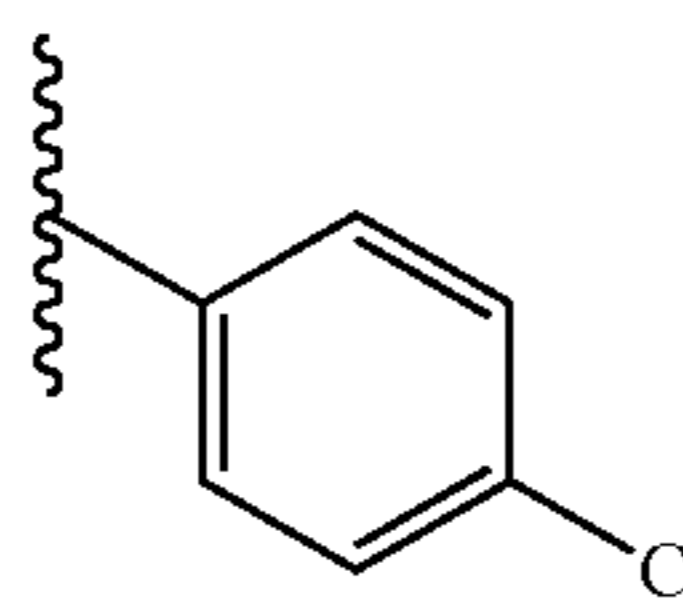
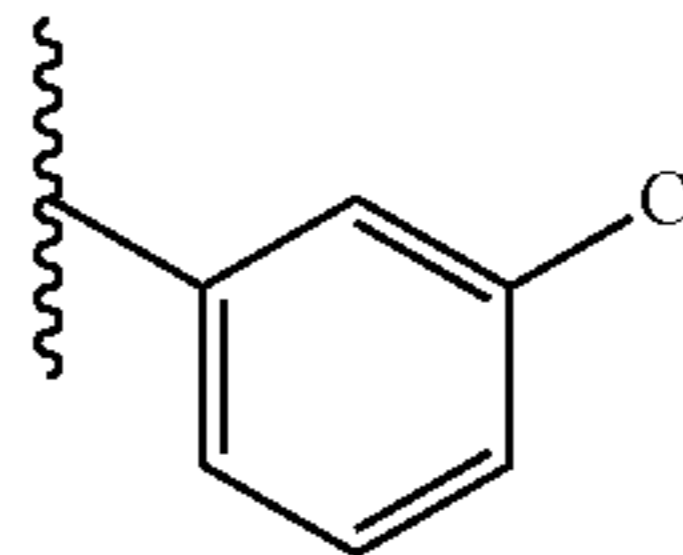
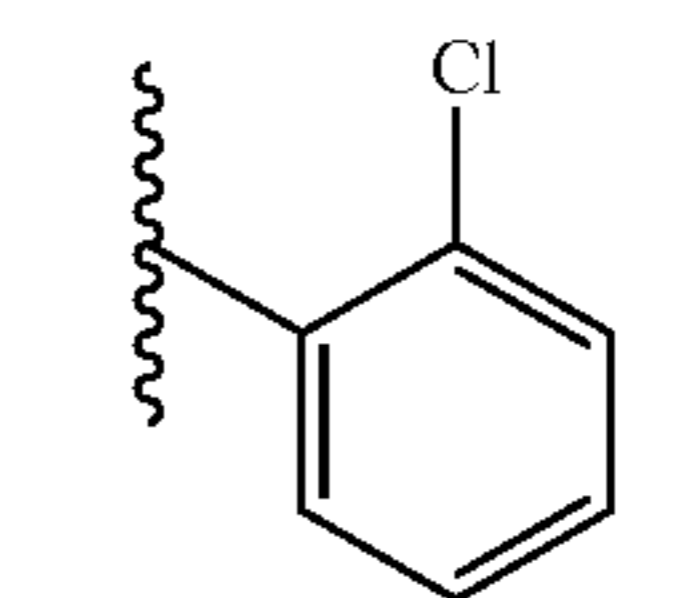
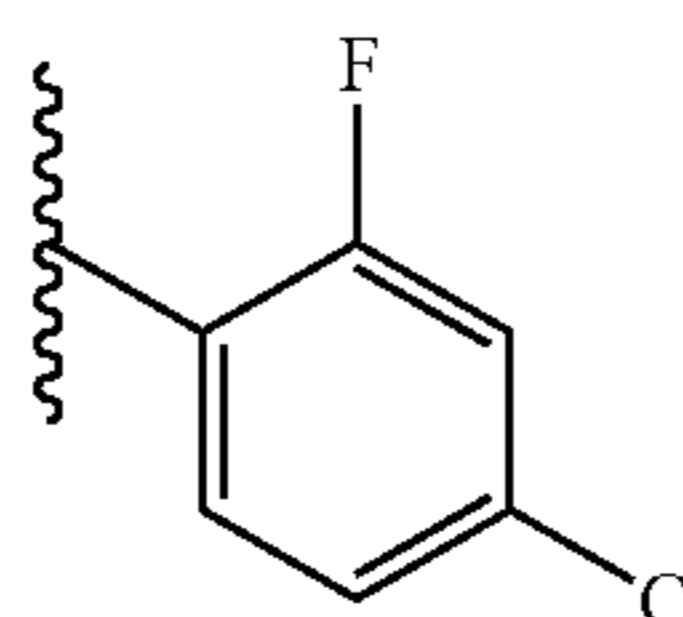
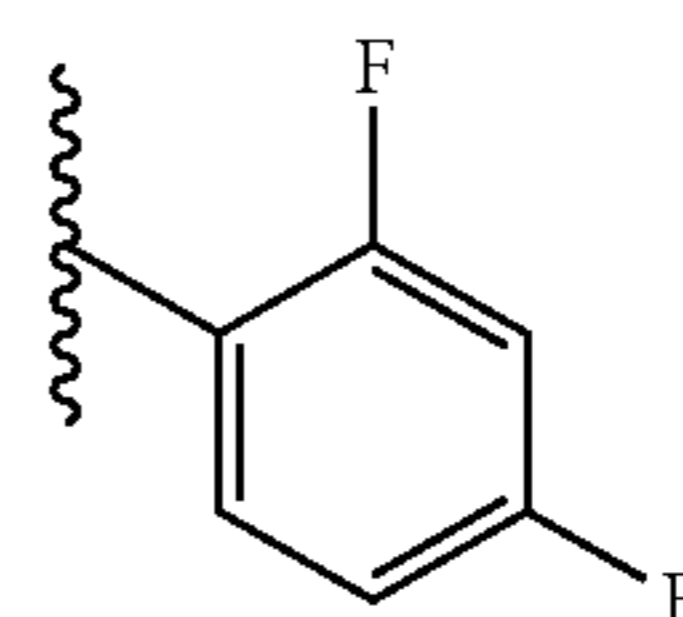
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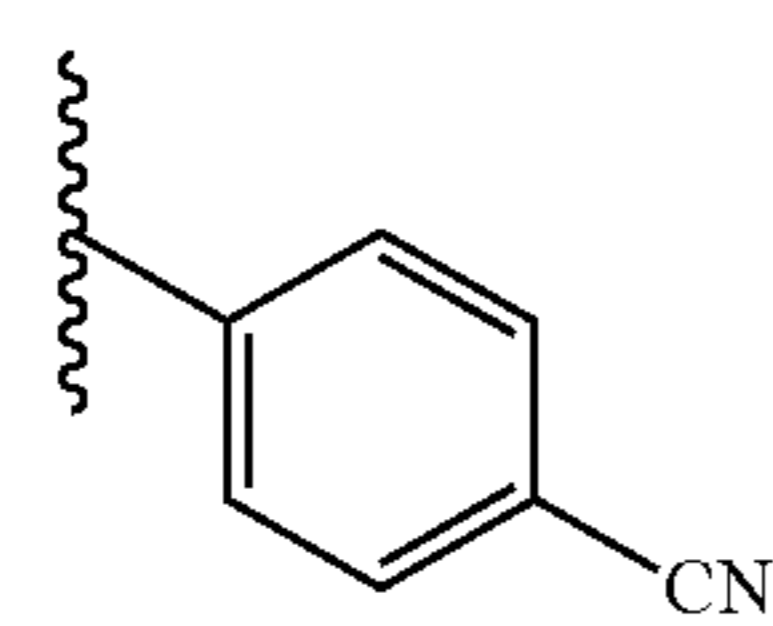
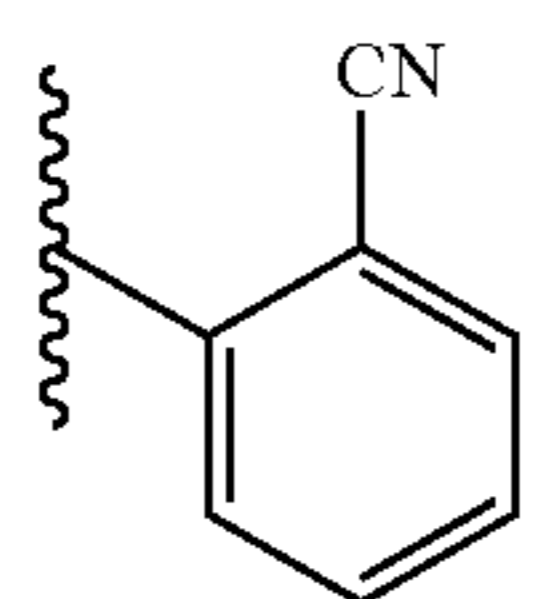
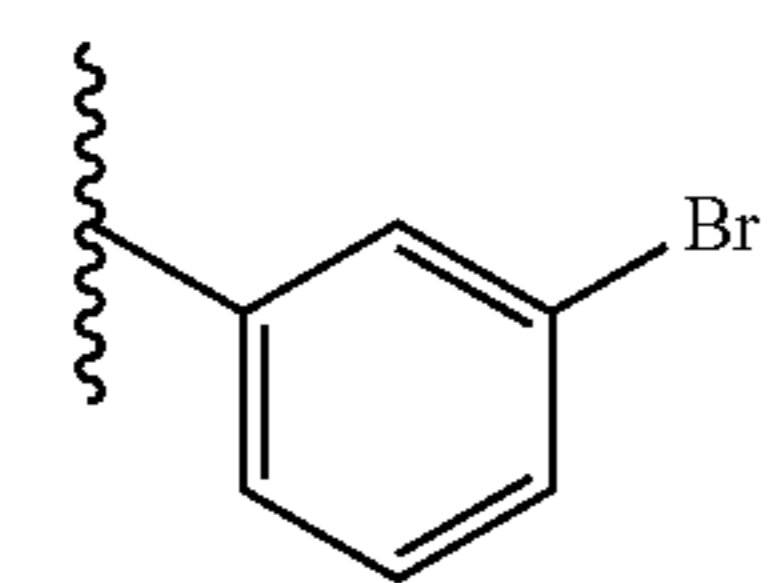
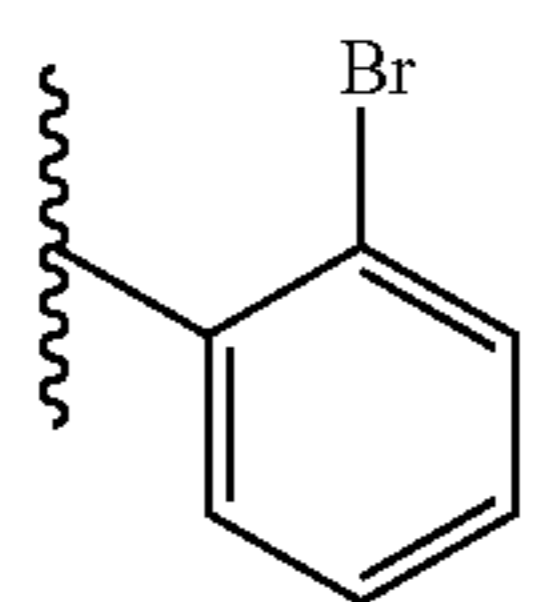
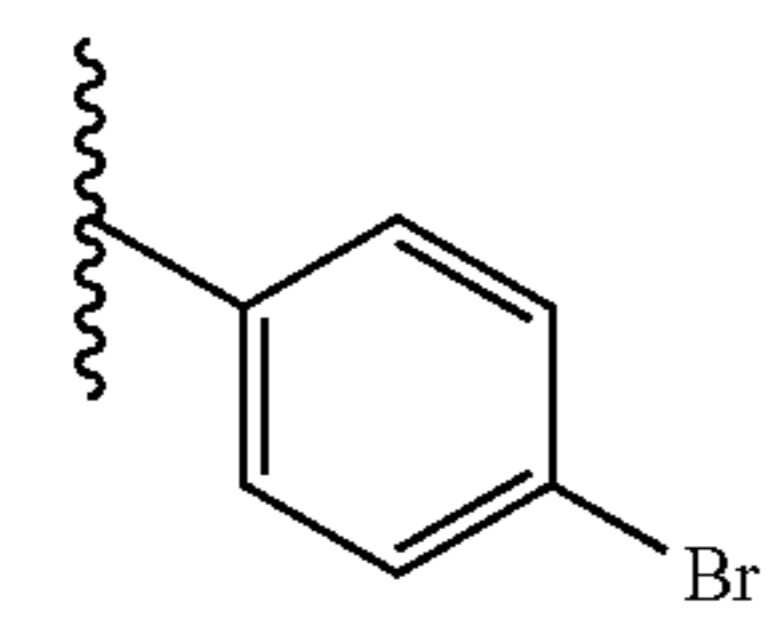
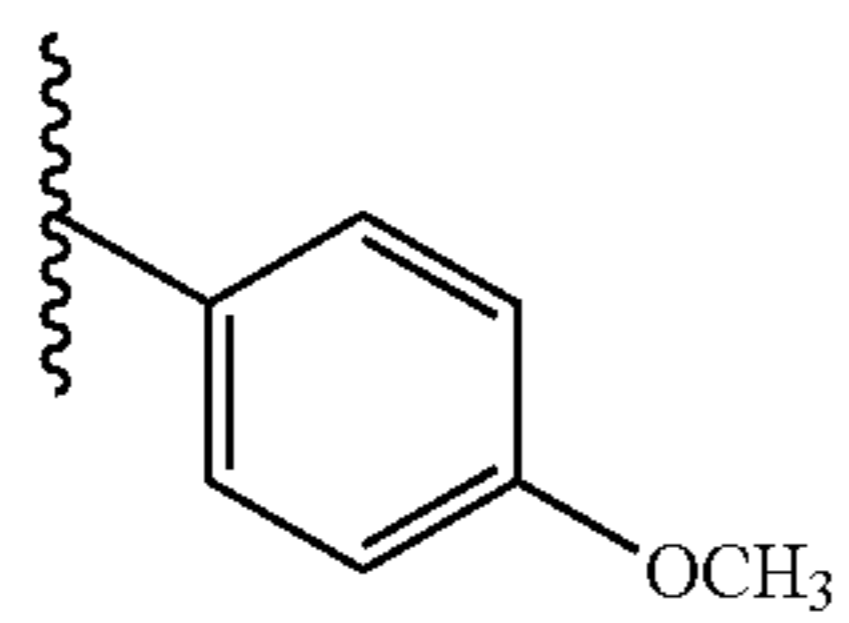
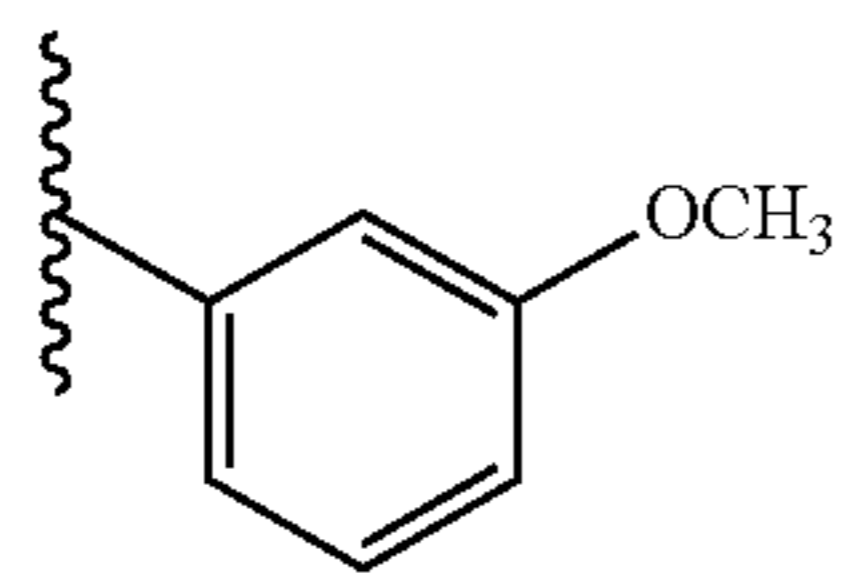
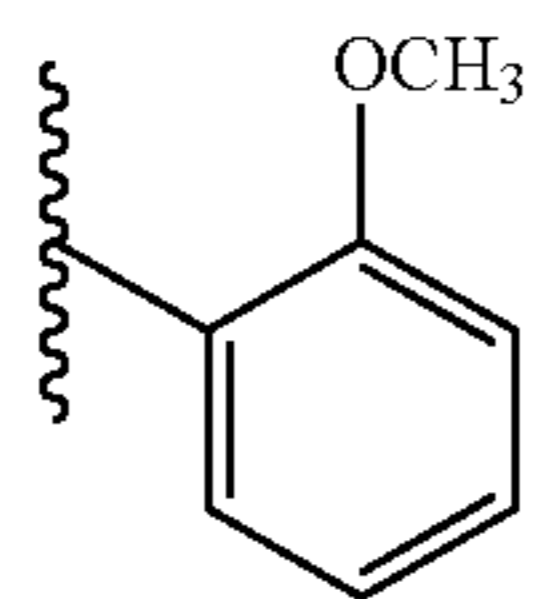
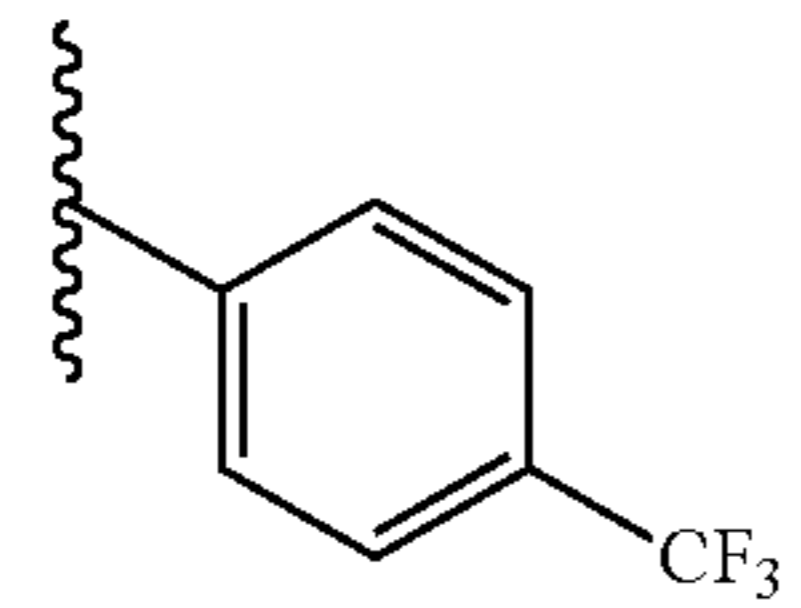
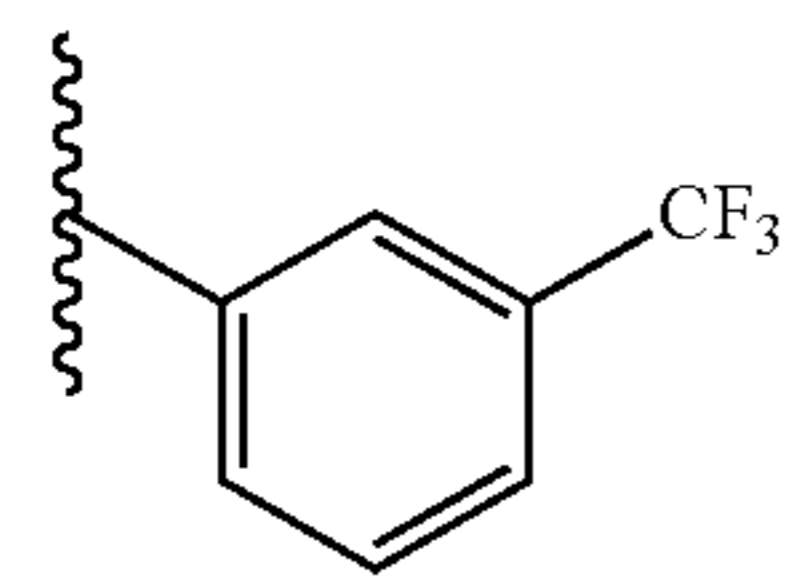
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TABLE 4-continued



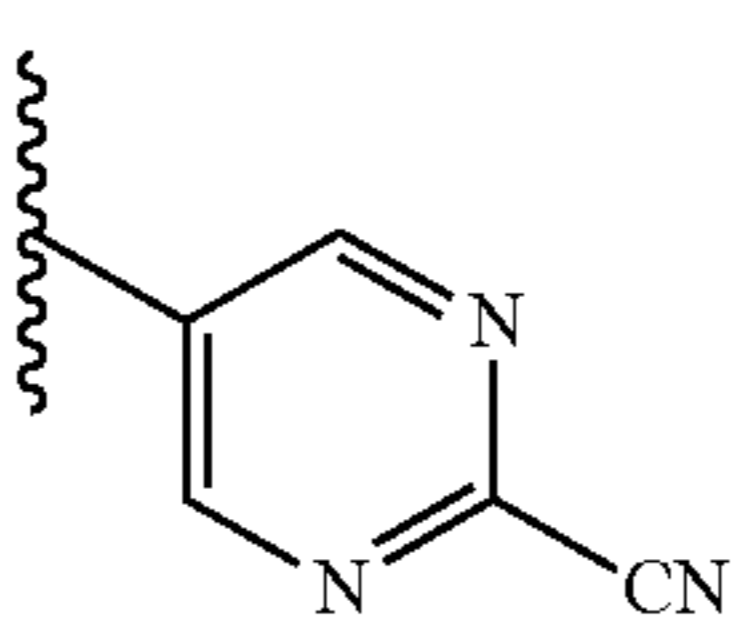
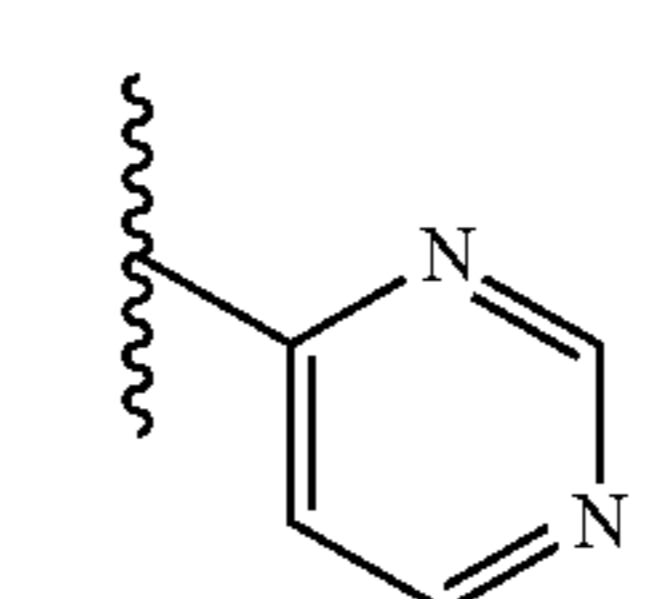
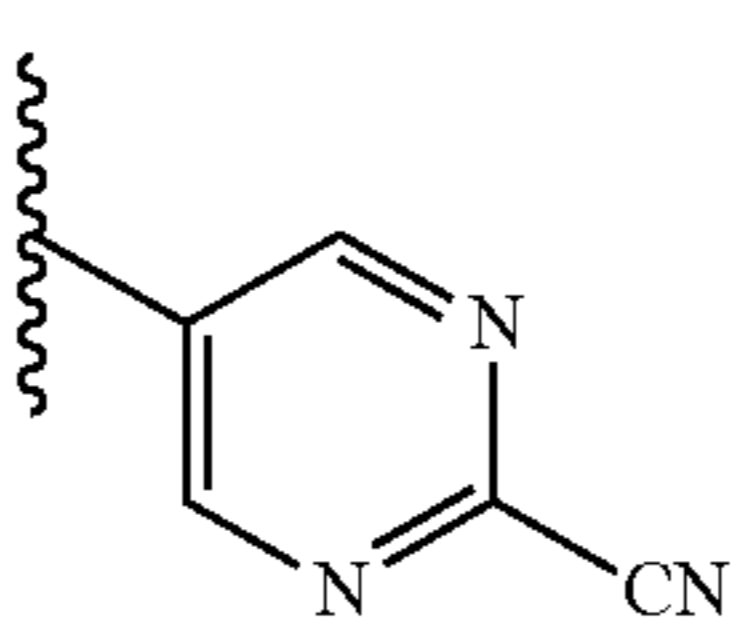
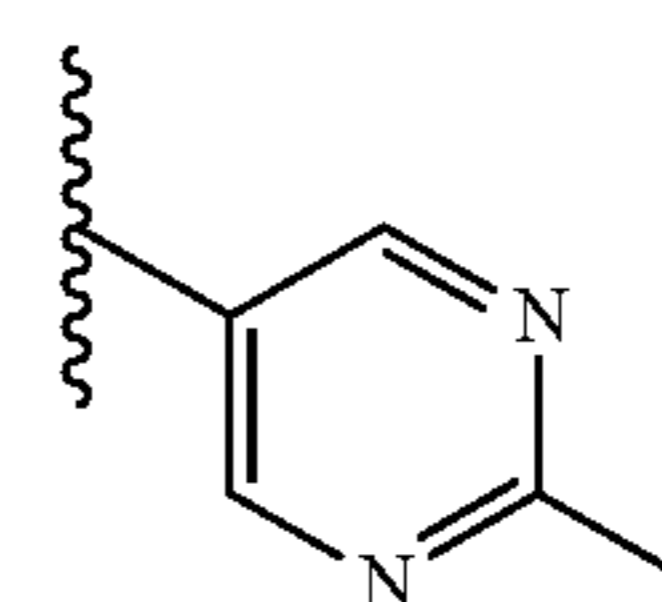
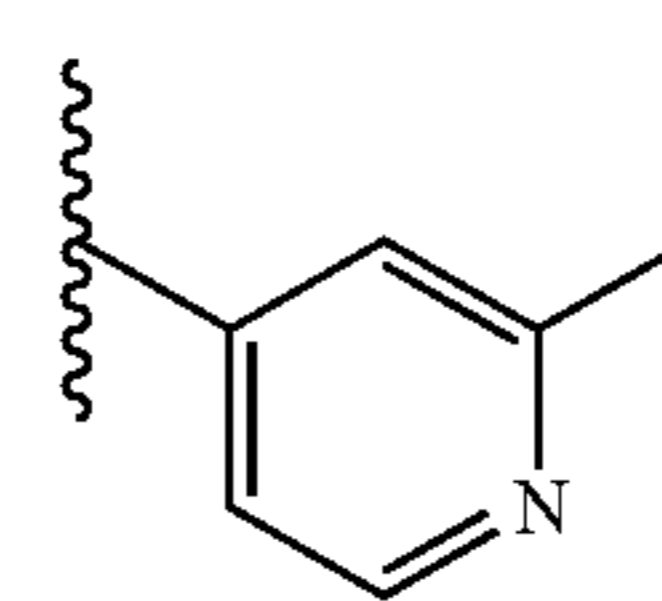
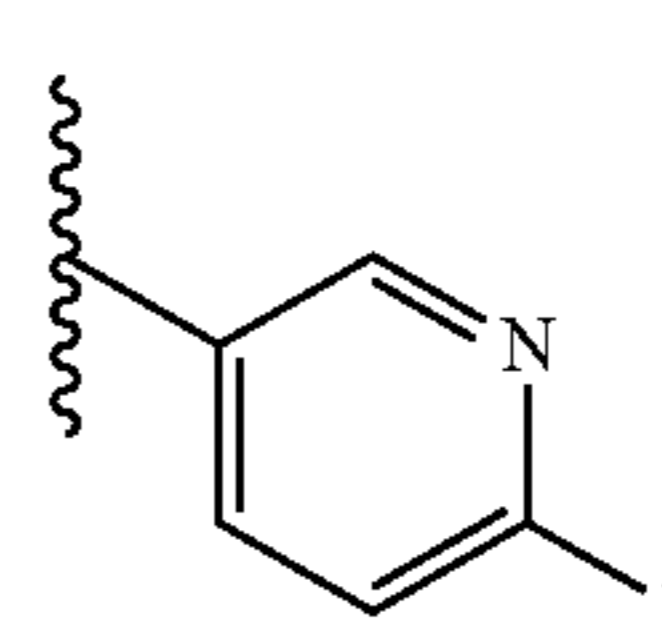
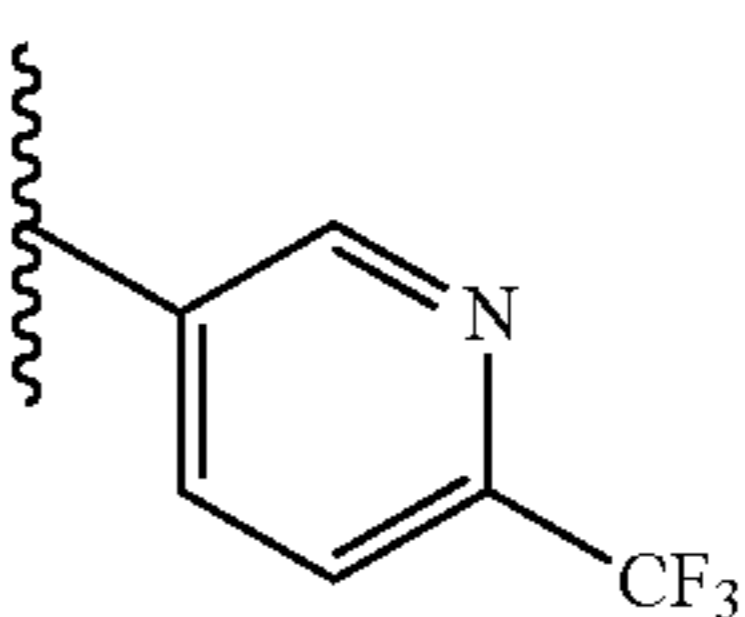
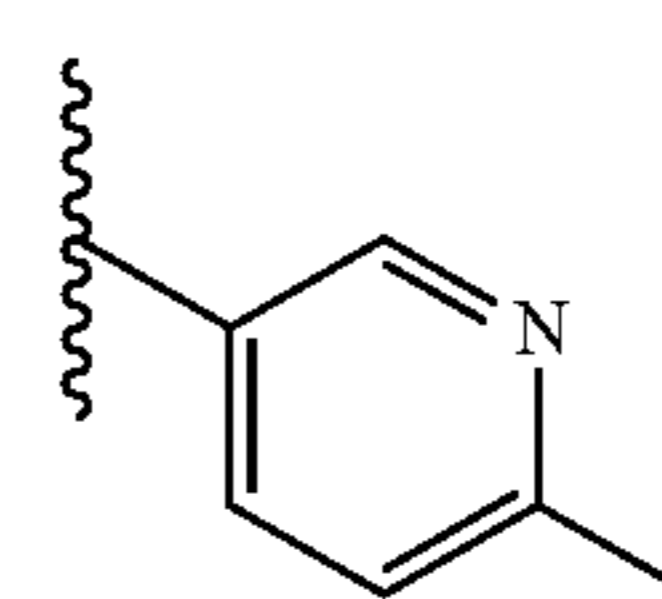
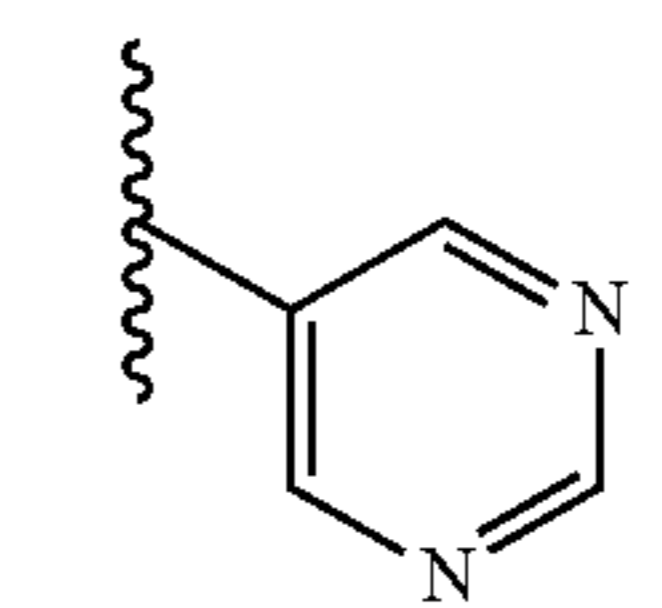
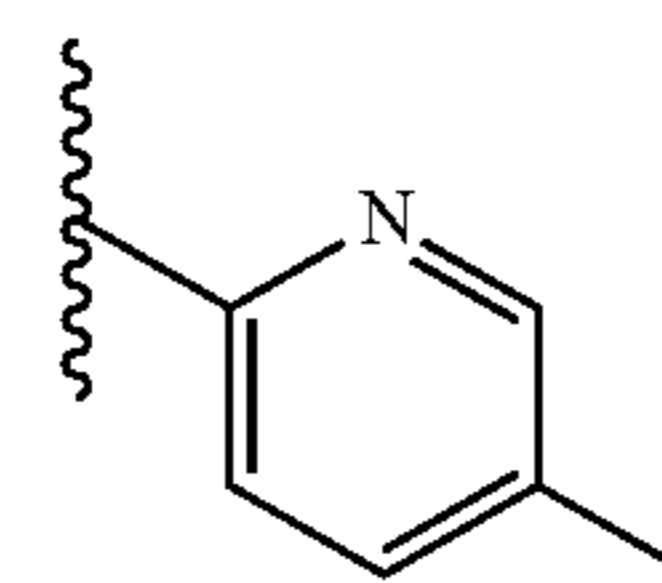
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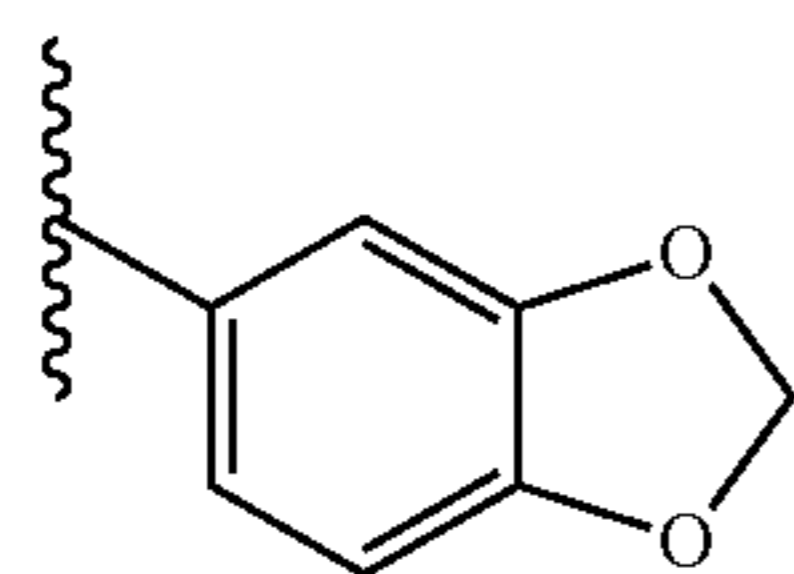
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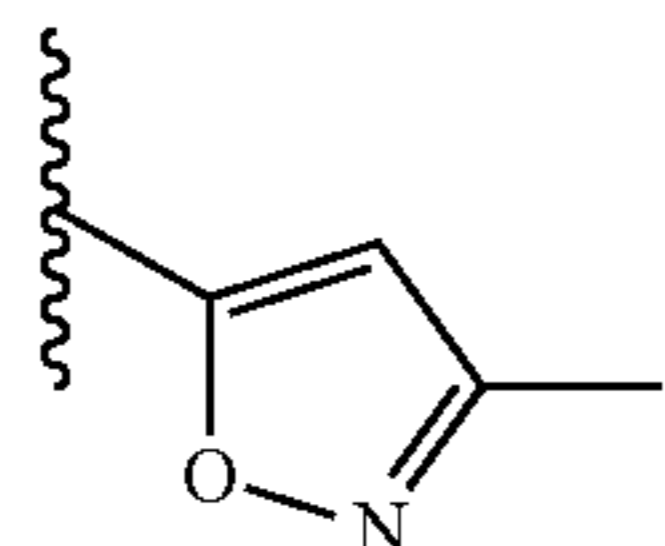


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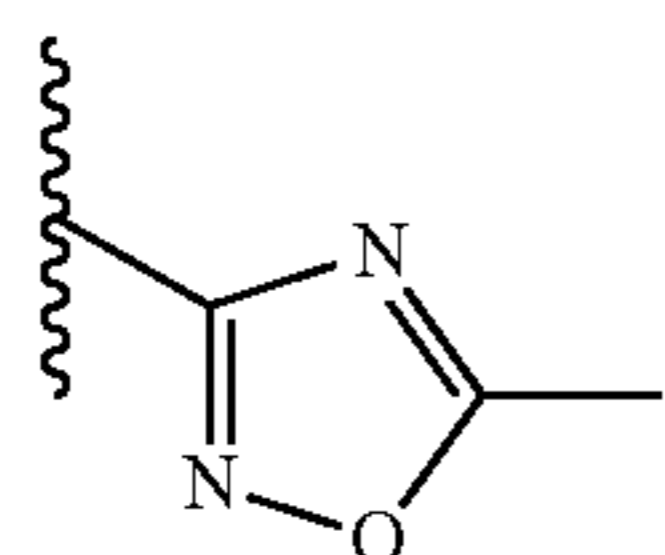
TABLE 4-continued



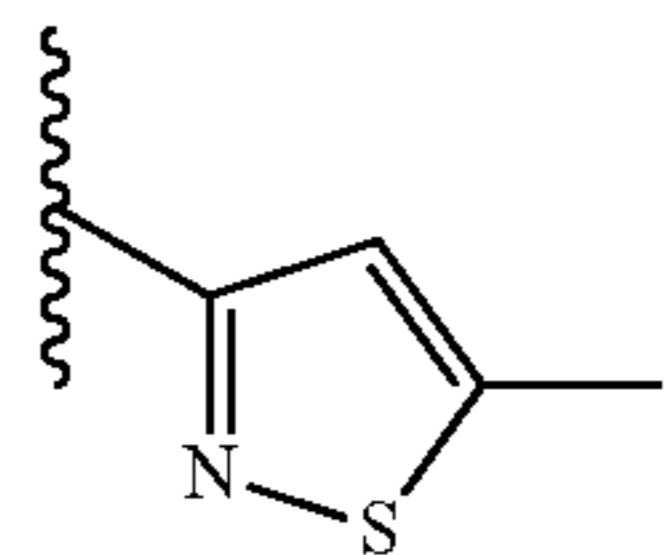
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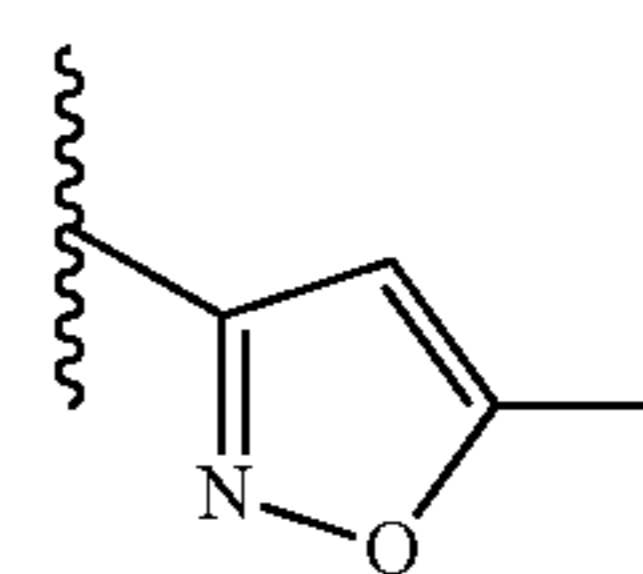
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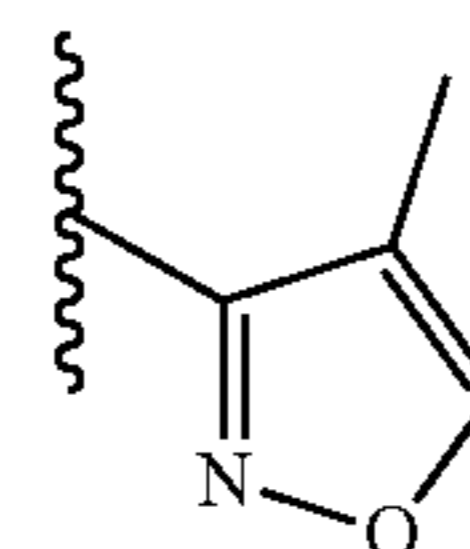
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TABLE 4-continued



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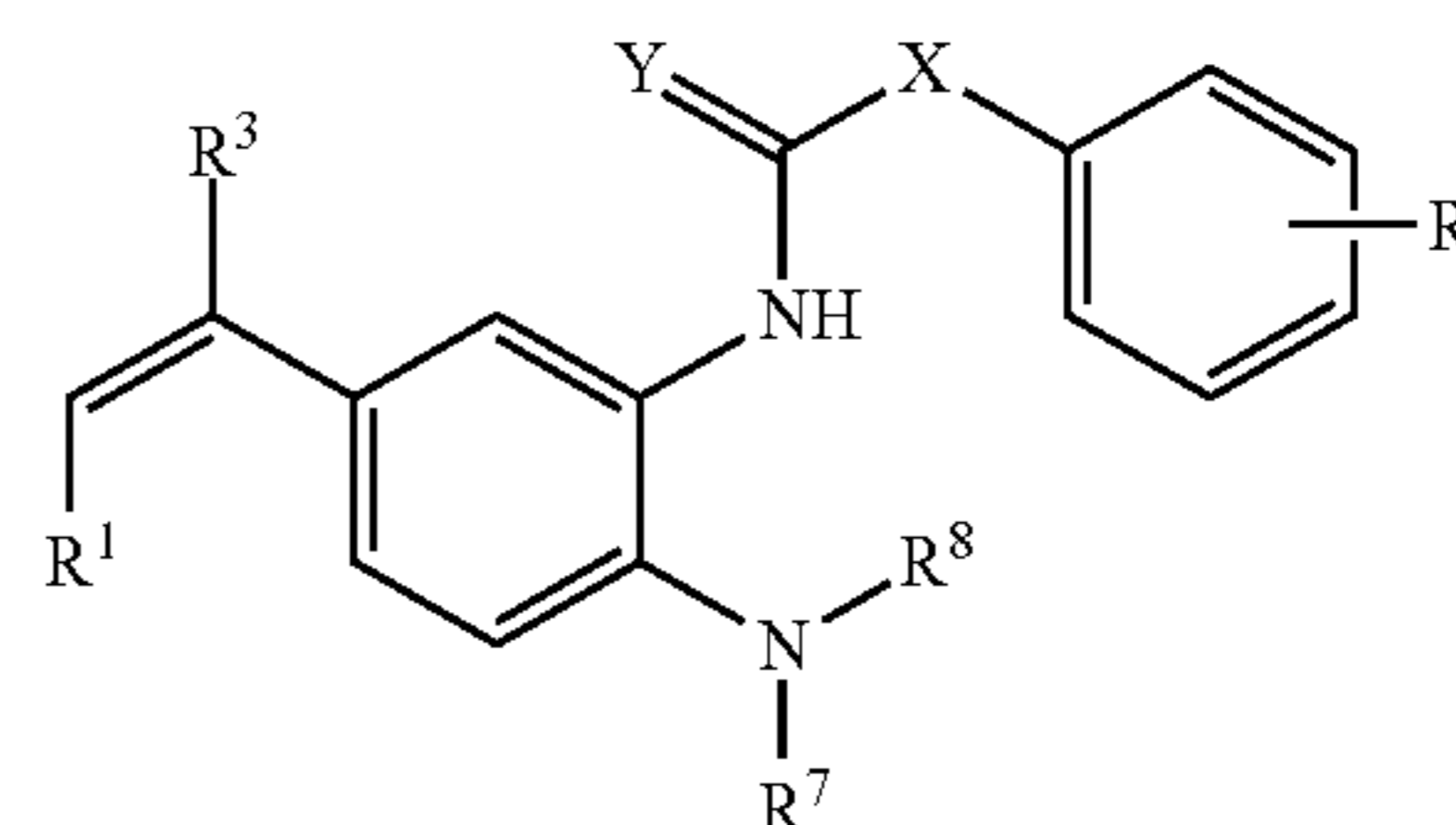
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In the present invention, the specific compound in formula I which inhibits the activity of the IDO enzyme is shown as formula II, The specific compound listed in table 5, but the present invention is not limited by these compounds

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Formula II

TABLE 5

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
1	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
2	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
3	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
4	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	NH
5	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	NH
6	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
7	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
8	COOH	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
9	COOH	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
10	COOH	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
11	COOH	CH ₃	n-butyl	n-butyl	2-F	O	NH
12	COOH	CH ₃	n-butyl	n-butyl	4-F	O	NH
13	COOH	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
14	COOH	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
15	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
16	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
17	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
18	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	NH
19	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	NH
20	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
21	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
22	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
23	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
24	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
25	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F	O	NH
26	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-F	O	NH
27	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
28	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
29	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
30	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
31	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
32	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	NH
33	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	NH
34	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
35	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
36	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
37	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
38	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
39	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	NH
40	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	NH
41	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
42	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
43	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
44	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
45	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
46	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	NH
47	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	NH
48	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
49	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
50	COOH	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
51	COOH	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
52	COOH	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
53	COOH	CH ₃	isobutyl	isobutyl	2-F	O	NH
54	COOH	CH ₃	isobutyl	isobutyl	4-F	O	NH
55	COOH	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
56	COOH	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
57	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
58	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
59	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
60	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	NH
61	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	NH
62	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
63	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
64	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
65	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
66	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
67	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F	O	NH
68	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-F	O	NH
69	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
70	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
71	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
72	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
73	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
74	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	NH
75	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	NH
76	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
77	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
78	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
79	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
80	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
81	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	NH
82	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	NH
83	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
84	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
85	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
86	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
87	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
88	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
89	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
90	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
91	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
92	COOH	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
93	COOH	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
94	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
95	COOH	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
96	COOH	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
97	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
98	COOH	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
99	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
100	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
101	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
102	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
103	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
104	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
105	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
106	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
107	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
108	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
109	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
110	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
111	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
112	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
113	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
114	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
115	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
116	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
117	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
118	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
119	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
120	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
121	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
122	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
123	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
124	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
125	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
126	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
127	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
128	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
129	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
130	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	NH
131	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	NH
132	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
133	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
134	COOH	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
135	COOH	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
136	COOH	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
137	COOH	CF ₃	n-butyl	n-butyl	2-F	O	NH
138	COOH	CF ₃	n-butyl	n-butyl	4-F	O	NH
139	COOH	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
140	COOH	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
141	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
142	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
143	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
144	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	NH
145	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	NH
146	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
147	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
148	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
149	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
150	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
151	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-F	O	NH
152	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	4-F	O	NH
153	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
154	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
155	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
156	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
157	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
158	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	NH
159	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	NH
160	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
161	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
162	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
163	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
164	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
165	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	NH
166	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	NH
167	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
168	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
169	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
170	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
171	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
172	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	NH
173	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	NH
174	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
175	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
176	COOH	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
177	COOH	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
178	COOH	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
179	COOH	CF ₃	isobutyl	isobutyl	2-F	O	NH
180	COOH	CF ₃	isobutyl	isobutyl	4-F	O	NH
181	COOH	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
182	COOH	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
183	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
184	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
185	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
186	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	NH
187	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	NH
188	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
189	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
190	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
191	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
192	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
193	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F	O	NH
194	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-F	O	NH
195	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
196	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
197	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
198	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
199	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
200	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	NH
201	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	NH
202	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
203	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
204	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
205	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
206	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
207	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	NH
208	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	NH
209	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
210	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
211	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
212	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
213	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
214	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
215	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
216	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
217	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
218	COOH	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
219	COOH	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
220	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
221	COOH	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
222	COOH	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
223	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
224	COOH	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
225	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
226	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
227	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
228	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
229	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
230	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
231	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
232	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
233	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
234	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
235	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
236	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
237	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
238	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
239	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
240	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
241	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
242	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
243	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
244	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
245	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
246	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
247	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
248	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
249	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
250	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
251	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
252	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
253	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
254	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
255	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
256	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
257	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
258	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
259	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
260	COOH	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
261	COOH	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
262	COOH	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
263	COOH	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
264	COOH	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
265	COOH	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
266	COOH	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
267	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
268	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
269	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
270	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
271	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
272	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
273	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
274	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
275	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
276	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
277	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
278	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
279	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
280	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
281	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
282	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
283	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
284	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
285	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
286	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
287	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
288	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
289	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
290	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
291	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
292	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
293	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
294	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
295	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
296	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
297	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
298	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
299	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
300	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
301	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
302	COOH	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
303	COOH	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
304	COOH	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
305	COOH	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
306	COOH	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
307	COOH	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
308	COOH	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
309	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
310	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
311	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
312	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
313	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
314	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
315	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
316	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
317	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
318	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
319	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
320	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
321	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
322	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
323	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
324	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
325	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
326	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
327	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
328	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
329	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
330	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
331	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
332	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
333	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
334	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
335	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
336	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
337	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
338	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
339	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
340	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
341	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
342	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
343	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
344	COOH	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
345	COOH	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
346	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
347	COOH	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
348	COOH	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
349	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
350	COOH	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
351	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
352	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
353	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
354	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
355	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
356	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
357	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
358	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
359	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
360	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
361	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
362	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
363	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
364	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
365	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
366	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
367	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
368	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
369	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
370	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
371	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
372	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
373	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
374	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
375	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
376	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
377	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
378	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
379	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
380	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
381	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
382	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
383	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
384	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
385	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
386	COOH	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
387	COOH	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
388	COOH	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
389	COOH	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
390	COOH	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
391	COOH	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
392	COOH	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
393	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
394	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
395	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
396	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
397	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
398	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
399	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
400	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
401	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
402	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
403	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
404	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
405	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
406	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
407	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
408	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
409	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
410	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
411	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
412	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
413	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
414	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
415	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
416	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
417	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
418	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
419	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
420	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
421	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
422	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
423	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
424	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
425	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
426	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
427	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
428	COOH	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
429	COOH	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
430	COOH	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
431	COOH	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
432	COOH	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
433	COOH	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
434	COOH	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
435	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
436	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
437	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
438	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
439	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
440	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
441	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
442	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
443	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
444	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
445	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
446	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
447	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
448	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
449	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
450	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
451	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
452	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
453	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
454	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
455	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
456	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
457	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
458	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
459	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
460	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
461	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
462	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
463	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
464	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
465	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
466	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
467	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
468	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
469	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
470	COOH	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
471	COOH	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
472	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
473	COOH	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
474	COOH	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
475	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
476	COOH	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
477	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
478	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
479	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
480	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
481	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
482	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
483	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
484	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
485	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
486	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
487	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
488	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
489	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
490	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
491	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
492	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
493	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
494	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
495	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
496	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
497	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
498	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂

TABLE 5-continued

Compound Number	R ¹	R ³	R ⁷	R ⁸	R	Y	X
499	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
500	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
501	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
502	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
503	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
504	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
505	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-Cl	O	NH
506	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	3-Cl	O	NH
507	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-Cl	O	NH
508	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	3-CF ₃ -4-Cl	O	NH
509	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	H	S	NH
510	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	3-CH ₃	O	NH
511	COOH	CH ₃	n-butyl	n-butyl	2-Cl	O	NH
512	COOH	CH ₃	n-butyl	n-butyl	3-Cl	O	NH
513	COOH	CH ₃	n-butyl	n-butyl	4-Cl	O	NH
514	COOH	CH ₃	n-butyl	n-butyl	3-CF ₃ -4-Cl	O	NH
515	COOH	CH ₃	n-butyl	n-butyl	H	S	NH
516	COOH	CH ₃	n-butyl	n-butyl	3-CH ₃	O	NH

In the present invention, the specific compound in formula I which inhibits the activity of the IDO enzyme is shown as formula III, The specific compound listed in table 6, but the present invention is not limited by these compounds. 25

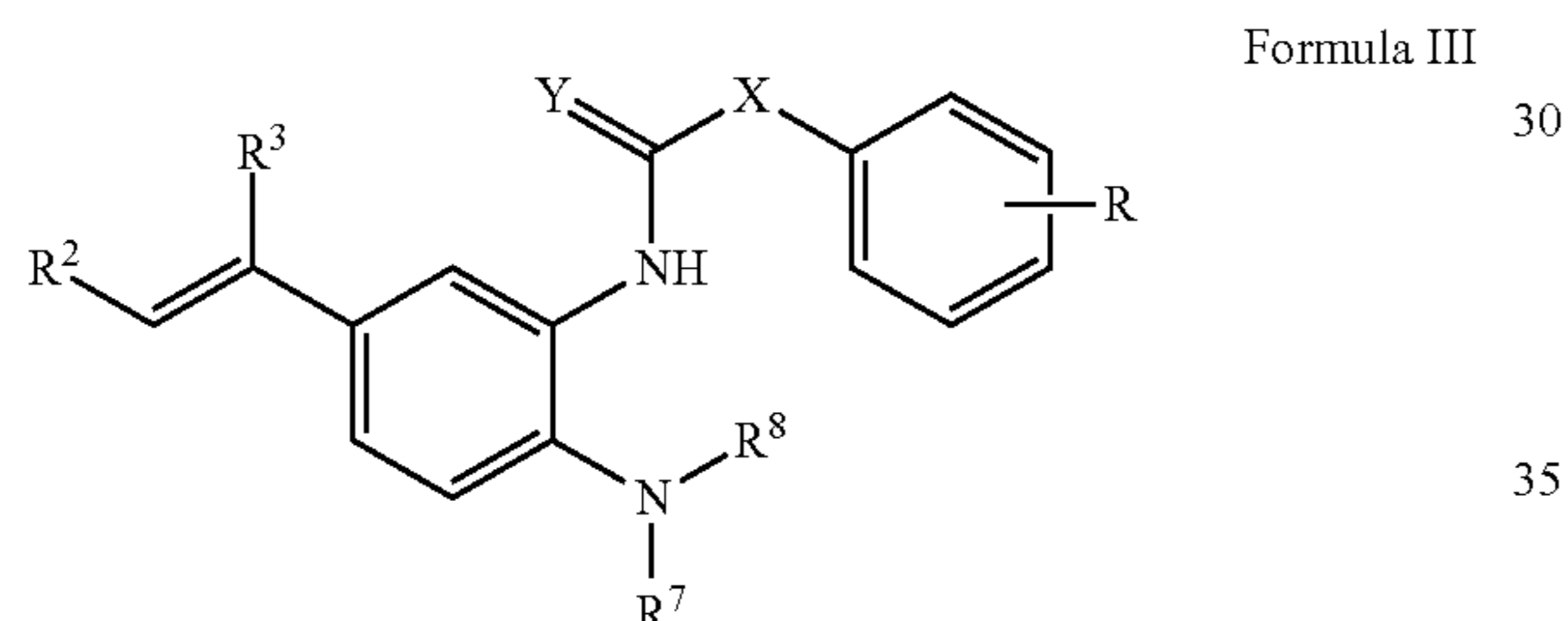


TABLE 6

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
517	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
518	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
519	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
520	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	NH
521	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	NH
522	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
523	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
524	COOH	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
525	COOH	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
526	COOH	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
527	COOH	CH ₃	n-butyl	n-butyl	2-F	O	NH
528	COOH	CH ₃	n-butyl	n-butyl	4-F	O	NH
529	COOH	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
530	COOH	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
531	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
532	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
533	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
534	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	NH
535	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	NH
536	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
537	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
538	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
539	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
540	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
541	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F	O	NH
542	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-F	O	NH
543	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
544	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
545	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH

TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
546	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
547	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
548	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	NH
549	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	NH
550	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
551	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
552	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	NH
553	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	NH
554	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
555	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	NH
556	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	NH
557	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	NH
558	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
559	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
560	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
561	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
562	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	NH
563	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	NH
564	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
565	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
566	COOH	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
567	COOH	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
568	COOH	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
569	COOH	CH ₃	isobutyl	isobutyl	2-F	O	NH
570	COOH	CH ₃	isobutyl	isobutyl	4-F	O	NH
571	COOH	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
572	COOH	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
573	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
574	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
575	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
576	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	NH
577	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	NH
578	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
579	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
580	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
581	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
582	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
583	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F	O	NH
584	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-F	O	NH
585	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
586	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
587	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
588	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
589	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
590	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	NH
591	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	NH
592	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
593	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
594	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	NH
595	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	NH
596	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
597	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	NH
598	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	NH
599	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	NH
600	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
601	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
602	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
603	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
604	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
605	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
606	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
607	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
608	COOH	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
609	COOH	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
610	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
611	COOH	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
612	COOH	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
613	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
614	COOH	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
615	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
616	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
617	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
618	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
619	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
620	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
621	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
622	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
623	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH

TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
624	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
625	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
626	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
627	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
628	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
629	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
630	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
631	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
632	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
633	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
634	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
635	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
636	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
637	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
638	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
639	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	NH
640	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	NH
641	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
642	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
643	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
644	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
645	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
646	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	NH
647	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	NH
648	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
649	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
650	COOH	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
651	COOH	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
652	COOH	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
653	COOH	CF ₃	n-butyl	n-butyl	2-F	O	NH
654	COOH	CF ₃	n-butyl	n-butyl	4-F	O	NH
655	COOH	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
656	COOH	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
657	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
658	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
659	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
660	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	NH
661	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	NH
662	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
663	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
664	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
665	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
666	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
667	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-F	O	NH
668	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	4-F	O	NH
669	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
670	CONHSO ₂ CF ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
671	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
672	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
673	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
674	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	NH
675	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	NH
676	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
677	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
678	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	NH
679	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	NH
680	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	NH
681	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	NH
682	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	NH
683	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	NH
684	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	NH
685	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
686	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
687	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
688	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	NH
689	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	NH
690	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
691	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
692	COOH	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
693	COOH	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
694	COOH	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
695	COOH	CF ₃	isobutyl	isobutyl	2-F	O	NH
696	COOH	CF ₃	isobutyl	isobutyl	4-F	O	NH
697	COOH	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
698	COOH	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
699	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
700	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
701	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH

TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
702	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	NH
703	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	NH
704	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
705	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
706	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
707	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
708	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
709	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F	O	NH
710	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-F	O	NH
711	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
712	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
713	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
714	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
715	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
716	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	NH
717	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	NH
718	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
719	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
720	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	NH
721	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	NH
722	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	NH
723	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	NH
724	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	NH
725	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	NH
726	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	NH
727	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
728	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
729	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
730	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
731	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
732	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
733	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
734	COOH	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
735	COOH	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
736	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
737	COOH	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
738	COOH	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
739	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
740	COOH	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
741	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
742	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
743	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
744	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
745	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
746	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
747	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
748	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
749	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
750	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
751	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
752	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
753	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
754	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
755	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
756	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
757	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
758	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
759	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
760	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
761	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
762	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	NH
763	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	NH
764	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	NH
765	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	NH
766	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	NH
767	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	NH
768	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	NH
769	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
770	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
771	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
772	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
773	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
774	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
775	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
776	COOH	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
777	COOH	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
778	COOH	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
779	COOH	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂

TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
780	COOH	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
781	COOH	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
782	COOH	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
783	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
784	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
785	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
786	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
787	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
788	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
789	CONHSO ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
790	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
791	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
792	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
793	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
794	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
795	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
796	CONHSO ₂ CF ₃	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
797	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
798	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
799	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
800	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
801	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
802	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
803	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
804	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
805	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
806	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
807	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F	O	CH ₂
808	5-tetrazolyl	CH ₃	n-butyl	n-butyl	4-F	O	CH ₂
809	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
810	5-tetrazolyl	CH ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
811	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
812	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
813	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
814	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
815	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
816	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
817	COOCH ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
818	COOH	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
819	COOH	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
820	COOH	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
821	COOH	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
822	COOH	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
823	COOH	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
824	COOH	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
825	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
826	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
827	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
828	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
829	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
830	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
831	CONHSO ₂ CH ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
832	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
833	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
834	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
835	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
836	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
837	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
838	CONHSO ₂ CF ₃	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
839	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
840	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
841	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
842	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
843	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
844	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
845	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
846	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
847	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
848	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
849	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F	O	CH ₂
850	5-tetrazolyl	CH ₃	isobutyl	isobutyl	4-F	O	CH ₂
851	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
852	5-tetrazolyl	CH ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
853	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
854	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
855	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
856	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
857	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂

TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
858	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
859	COOCH ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
860	COOH	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
861	COOH	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
862	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
863	COOH	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
864	COOH	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
865	COOH	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
866	COOH	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
867	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
868	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
869	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
870	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
871	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
872	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
873	CONHSO ₂ CH ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
874	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
875	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
876	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
877	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
878	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
879	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
880	CONHSO ₂ CF ₃	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
881	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
882	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
883	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
884	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
885	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
886	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
887	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
888	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
889	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
890	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
891	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
892	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
893	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
894	5-tetrazolyl	CH ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
895	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
896	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
897	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
898	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
899	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
900	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
901	COOCH ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
902	COOH	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
903	COOH	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
904	COOH	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
905	COOH	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
906	COOH	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
907	COOH	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
908	COOH	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
909	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
910	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
911	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
912	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
913	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
914	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
915	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
916	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
917	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
918	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
919	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
920	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
921	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
922	CONHSO ₂ CH ₃	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
923	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
924	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
925	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
926	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
927	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
928	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂
929	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
930	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-CH ₃	O	CH ₂
931	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-CH ₃	O	CH ₂
932	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2CH ₃	O	CH ₂
933	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F	O	CH ₂
934	5-tetrazolyl	CF ₃	n-butyl	n-butyl	4-F	O	CH ₂
935	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2,4-2F	O	CH ₂

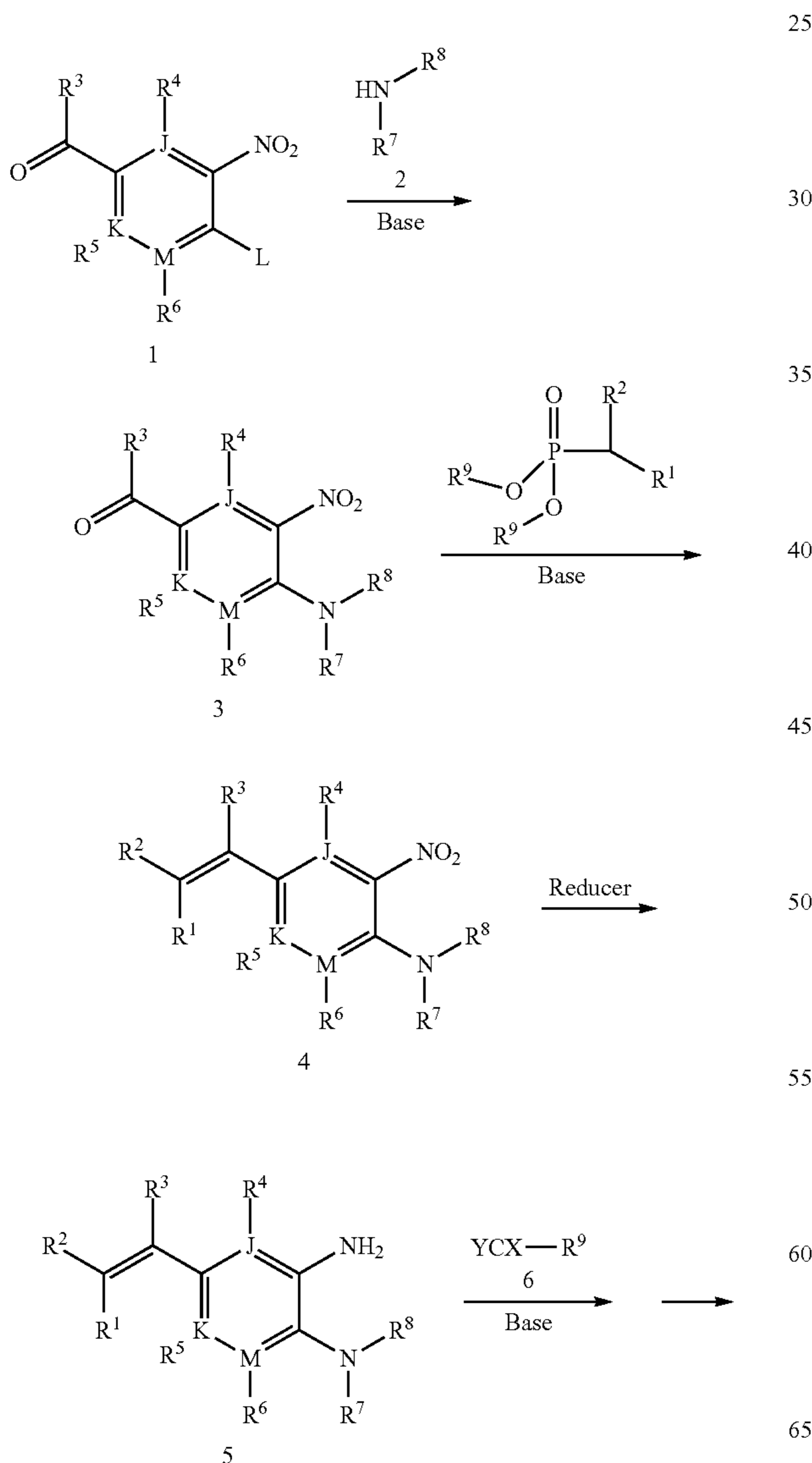
TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
936	5-tetrazolyl	CF ₃	n-butyl	n-butyl	2-F-4-CH ₃	O	CH ₂
937	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
938	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
939	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
940	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
941	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
942	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
943	COOCH ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
944	COOH	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
945	COOH	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
946	COOH	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
947	COOH	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
948	COOH	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
949	COOH	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
950	COOH	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
951	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
952	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
953	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
954	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
955	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
956	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
957	CONHSO ₂ CH ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
958	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
959	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
960	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
961	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
962	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
963	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
964	CONHSO ₂ CF ₃	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
965	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
966	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
967	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
968	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
969	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
970	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
971	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
972	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-CH ₃	O	CH ₂
973	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-CH ₃	O	CH ₂
974	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2CH ₃	O	CH ₂
975	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F	O	CH ₂
976	5-tetrazolyl	CF ₃	isobutyl	isobutyl	4-F	O	CH ₂
977	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2,4-2F	O	CH ₂
978	5-tetrazolyl	CF ₃	isobutyl	isobutyl	2-F-4-CH ₃	O	CH ₂
979	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
980	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
981	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
982	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
983	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
984	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
985	COOCH ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
986	COOH	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
987	COOH	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
988	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
989	COOH	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
990	COOH	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
991	COOH	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
992	COOH	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
993	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
994	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
995	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
996	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
997	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
998	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
999	CONHSO ₂ CH ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
1000	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
1001	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
1002	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
1003	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
1004	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
1005	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
1006	CONHSO ₂ CF ₃	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂
1007	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
1008	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
1009	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
1010	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
1011	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
1012	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
1013	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4-CH ₃	O	CH ₂

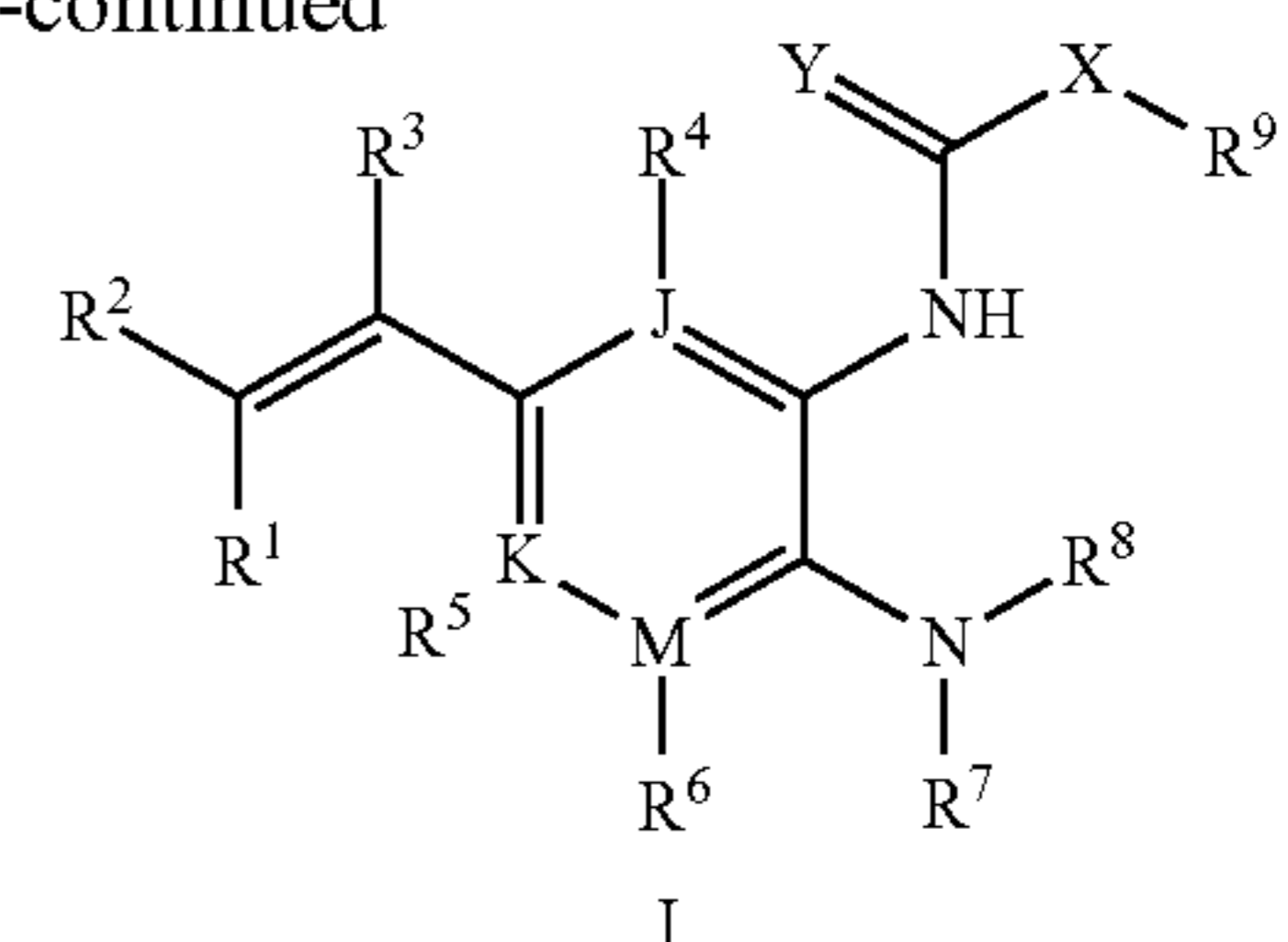
TABLE 6-continued

Compound Number	R ²	R ¹	R ⁷	R ⁸	R	Y	X
1014	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-CH ₃	O	CH ₂
1015	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-CH ₃	O	CH ₂
1016	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2CH ₃	O	CH ₂
1017	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F	O	CH ₂
1018	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	4-F	O	CH ₂
1019	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2,4-2F	O	CH ₂
1020	5-tetrazolyl	CF ₃	cyclohexyl	isobutyl	2-F-4CH ₃	O	CH ₂
1021	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	2-Cl	O	NH
1022	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	3-Cl	O	NH
1023	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	4-Cl	O	NH
1024	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	3-CF ₃ 4-Cl	O	NH
1025	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	H	S	NH
1026	COOCH ₂ CH ₃	CH ₃	n-butyl	n-butyl	3-CH ₃	O	NH
1027	COOH	CH ₃	n-butyl	n-butyl	2-Cl	O	NH
1028	COOH	CH ₃	n-butyl	n-butyl	3-Cl	O	NH
1029	COOH	CH ₃	n-butyl	n-butyl	4-Cl	O	NH
1030	COOH	CH ₃	n-butyl	n-butyl	3-CF ₃ 4-Cl	O	NH
1031	COOH	CH ₃	n-butyl	n-butyl	H	S	NH
1032	COOH	CH ₃	n-butyl	n-butyl	3-CH ₃	O	NH

The formula I compound of the invention can be prepared according to the following methods:



-continued



In the above reaction formula, the commercial halo nitroaromatic ketone compound 1 reacts with the substituted amino compound 2 to form the substituted amino nitroaromatic ketone compound 3 under the alkaline condition. Compound 3 reacts with wittingene reagent to form aromatic ethylene compound 4 under the alkaline condition. Compound 4 is reduced to amino compound 5 under the condition of reducing agent. Compound 5 reacts with compound 6 (isocyanate, isothiocyanate and chloroformate) to form formula I compound.

In the scheme:

L is selected from halogen, where L=F, Cl, Br and I; the definitions of the other groups are the same as before.

Base is selected from KOH, NaOH, Na₂CO₃, K₂CO₃, NaHCO₃, Et₃N, pyridine, MeONa, EtONa, NaH, potassium tert-butoxide or sodium tert-butoxide and so on.

The reaction is carried out in a suitable solvent, solvent is selected from THF, MeCN, PhMe, Xylene, Benzene, DMF, DMSO, acetone or methyl ethyl ketone and so on.

The reaction temperature may be between room temperature and the boiling point of the solvent, usually from 20 to 100° C.

The reaction time is from 30 minutes to 20 hours, usually from 1 to 10 hours.

The invention includes a formulation prepared by using the compound contained in the formula I as an active ingredient and other preparations. The preparation method of the formulation is as follows: dissolving the compound of the invention into a water-soluble organic solvent, a non-ionic surfactant, a water-soluble lipid, various cyclodextrins, a fatty acid, a fatty acid ester, a phospholipid or their combined solvents to prepare a preparation solution; adding normal saline to get 1-20% carbohydrates. The organic

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solvent includes one or a combination of polyethylene glycol (PEG), ethanol, propylene glycol and the like.

The compound shown in formula I of the present invention, its stereoisomer, cis-trans isomer, tautomer and pharmaceutically acceptable salt thereof, or a combination thereof, in the preparation of an inhibitor for inhibiting the activity of IDO-1 enzyme.

The compound shown in formula I of the present invention, its stereoisomer, cis-trans isomer, tautomer and pharmaceutically acceptable salt thereof, or a combination thereof, in the preparation of an anti-cancer drug, a viral infectious agent, a depressant, an organ transplant rejection agent or an autoimmune enhancer.

The cancer referred to is colon cancer, liver cancer, lymphoma, lung cancer, esophageal cancer, breast cancer, central nervous system tumor, melanoma, ovarian cancer, cervical cancer, renal cancer, leukemia, prostate cancer, pancreatic cancer or gastric cancer.

A pharmaceutical composition, any one or more compounds of formula I, its stereoisomer, cis-trans isomer, tautomer, pharmaceutically acceptable salts thereof and pharmaceutically acceptable carriers or diluents.

The compound of the present invention can be used as an active ingredient of an antitumor drug, and can be used alone or in combination with other antitumor drugs. The combination therapy referred to herein includes the use of at least one compound of the invention and a reactive derivative thereof in combination with one or more other anti-tumor agents to increase overall efficacy. The dose and time of administration in combination should be determined according to the most reasonable therapeutic effect obtained under different conditions.

The pharmaceutical agents contemplated include an effective dose of a compound of formula I. By "effective amount" herein is meant the amount of the compound required to produce a therapeutic effect for the subject being treated. The effective dose or dose can be varied by an experienced person depending on the recommendations of the situation. For example, the type of tumor treated is different, the usage of the drug is different; whether it is shared with other treatment methods such as other anti-tumor drugs, the dosage can be changed. Any application formulation form that can be made. If some of them have a basic or acidic compound and can form a non-toxic acid or salt, the form of the salt of the compound can be used. The carboxylic acid compound may form a usable salt with an alkali metal or an alkaline earth metal.

The compounds encompassed by the formula I in the invention are generally soluble in organic solvents, water-soluble solvents, organic solvents or a mixed solvent of a water-soluble solvent and water. The water-soluble solvent is preferably alcohol, polyethylene glycol, N-methyl-2-pyrrolidinone, DMA, DMF, DMSO, acetonitrile and their combination. The alcohol is preferably methanol, ethanol, isopropanol, glycerol or ethylene glycol. The compound of the present invention can be formulated into a preparation by mixing with usual formulation carriers. The compound is dissolved in a water-soluble organic solvent, an aprotic solvent, a water-soluble lipid, a cyclodextrin, a fatty acid, a phospholipid or a mixed solvent of these solvents to prepare a drug solution; and then adding physiological saline to obtain 1-20% carbohydrates, such as an aqueous solution of glucose. The formulations thus prepared are stable and are used in animals and clinical trials.

The product drug prepared by using the compound of the formula I as an active ingredient can be administered by oral or parenteral route, or can be administered by a drug pump

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in vivo and other methods. The non-intestinal route refers to subcutaneous intradermal, intramuscular, intravenous, intraarterial, intraatrial, synovial, sternal, intrathecal, traumatic site, intracranial injection or drip technology and so on. Professional person uses a conventional method to mix and mix and finally become the desired pharmaceutical dosage form. It may be a tablet, a capsule, an emulsion, a powder, a small needle for intravenous administration, a large infusion, a lyophilized powder, a dropping pill, a milk suspension, an aqueous suspension solution, an aqueous solution, a colloid, a colloidal solution, a sustained release preparation, a nano preparation or other forms of the dosage form are for animal or clinical use.

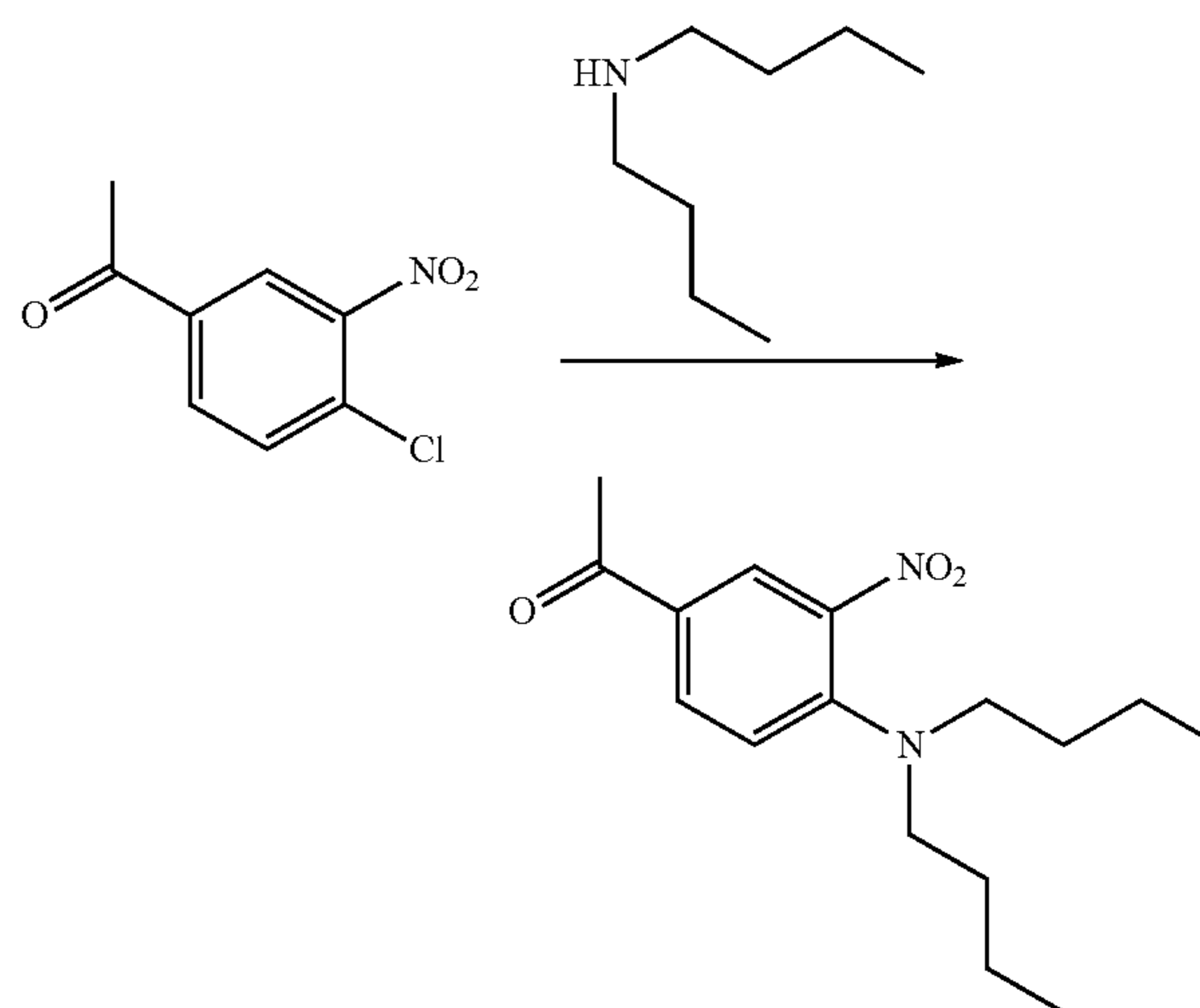
The compound of formula I of the invention is useful for the treatment or amelioration of cancer drugs for a certain tissue or organ. The cancers referred to include, but are not limited to, colon cancer, liver cancer, lymphoma, lung cancer, esophageal cancer, breast cancer, central nervous system tumor, melanoma, ovarian cancer, renal cancer, leukemia, prostate cancer or pancreatic cancer.

The invention has the advantages of having IDO-1 enzyme inhibitory activity and is expected to provide a novel therapeutic method and scheme for the related diseases caused by the IDO enzyme.

THE DETAILED DESCRIPTION OF THE INVENTION

The following examples are provided to assist in a comprehensive understanding of the claims and their equivalents, and are not intended to limit the present invention.

Example 1



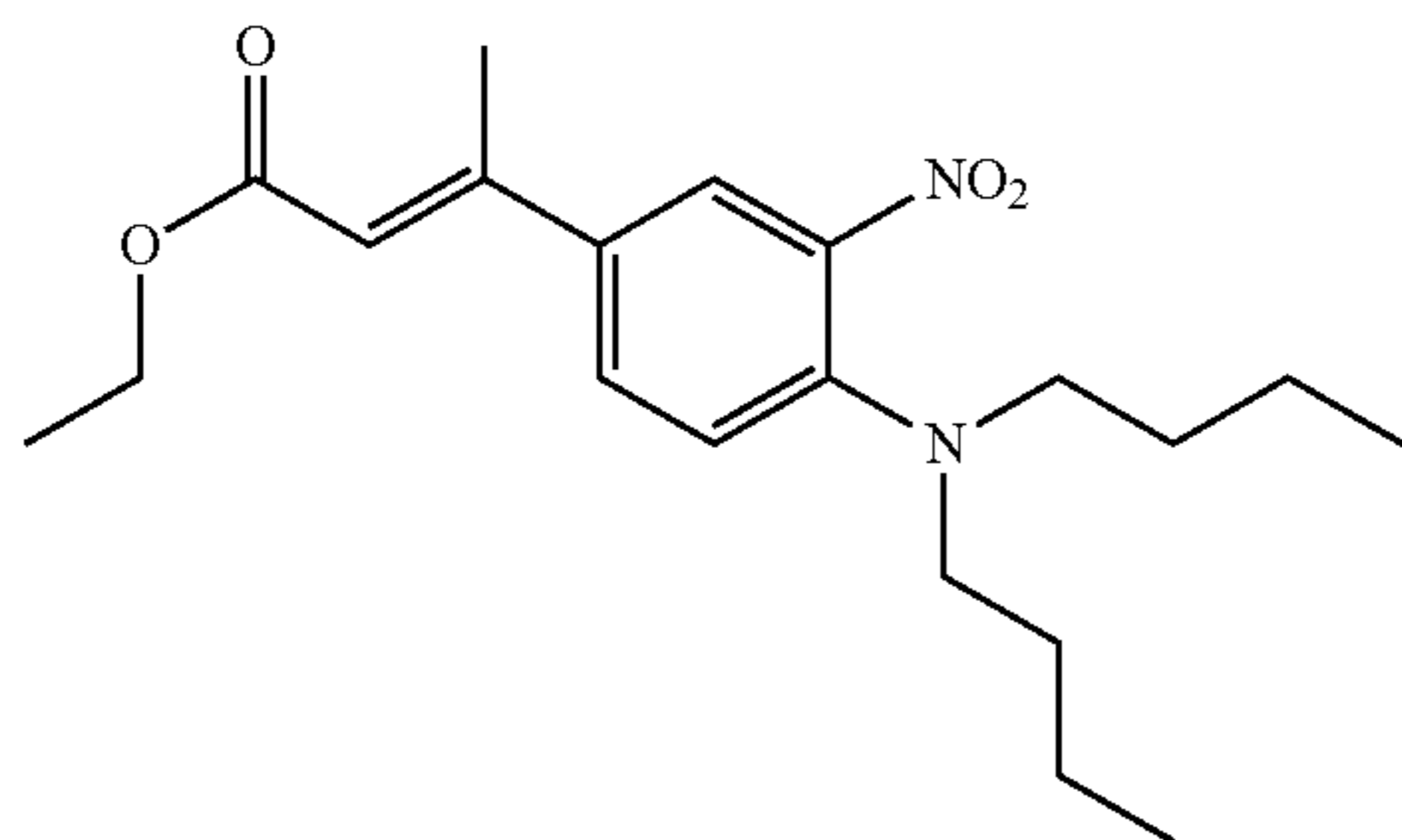
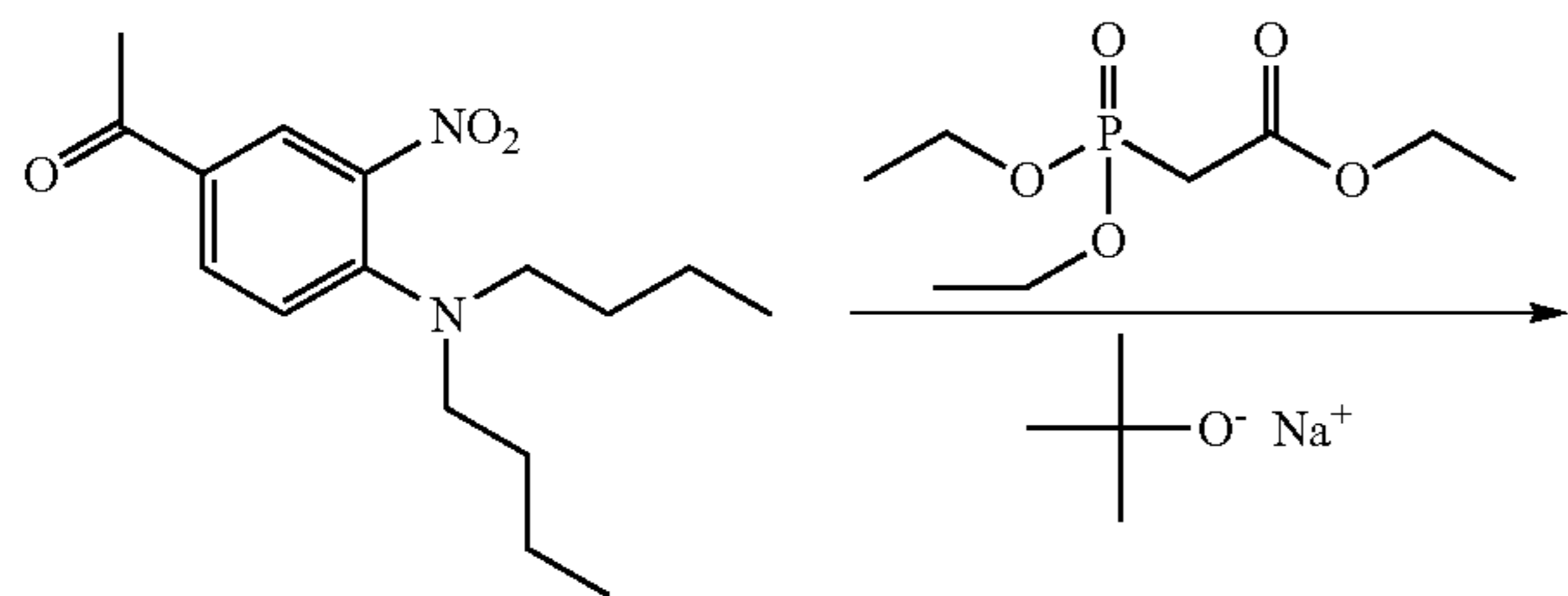
To a 250 mL flask, 10.0 g of 3'-nitro-4'-chloroacetophenone and 100 mL of di-n-butylamine were added, and the mixture was heated at 100° C. for 20 hours. After reaction was completed by TLC monitoring, the reaction mixture was evaporated to dryness, and the residue was dissolved in ethyl acetate (300 mL) and washed with water (100 mL×3), and the organic phase was dried over anhydrous sodium sulfate for 12 hr. The solvent was removed in vacuo. purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.)),

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the volume ratio is 1:6)) to obtain the compound 1-(4-(dibutylamino)-3-nitrophenyl)ethan-1-one, 11.3 g yellow solid.

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 0.89 (t, $J=7.5$ Hz, 6H), 1.23-1.35 (m, 4H), 1.52-1.62 (m, 4H), 2.51 (s, 3H), 3.23 (t, $J=7.2$ Hz, 4H), 7.08 (dd, $J=14.4, 3.9$ Hz, 1H), 7.96 (dd, $J=9.0, 2.1$ Hz, 1H), 8.31 (dd, $J=2.1$ Hz, 1H).

Example 2

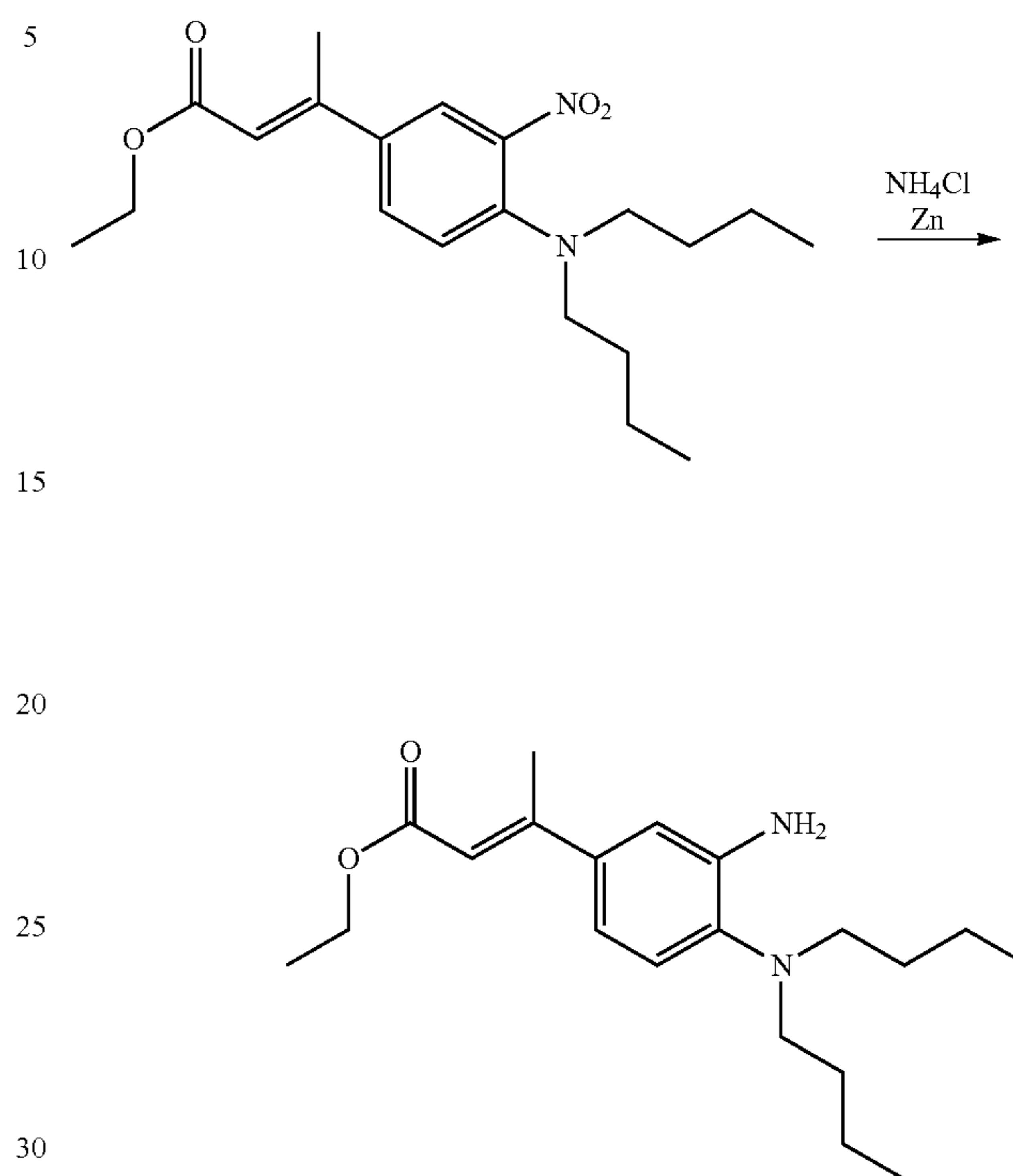


To a 250 mL flask, 9.9 g of sodium t-butoxide and 150 mL of tetrahydrofuran were added, and 23.0 g of ethyl 2-(diethoxyphosphoryl)acetate was added dropwise with stirring at a temperature of 0 to 5° C. After the dropwise addition completely, the mixture was stirred at room temperature for 0.5 hour, and the compound 1-(4-(dibutylamino)-3-nitrophenyl)ethan-1-one dissolved in 50 mL of tetrahydrofuran was added dropwise with stirring at a temperature of 20-30° C. After the dropwise addition completely, the mixture was stirred at room temperature for 12 hours. After reaction was completed by TLC monitoring, the reaction mixture was washed with a saturated aqueous solution of ammonium chloride (100 mL \times 3), and the organic phase was dried over anhydrous sodium sulfate for 12 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent ethyl acetate and petroleum ether (boiling range 60-90° C.), volume ratio 1:10) to obtain the compound ethyl (E)-3-(4-(dibutylamino)-3-nitrophenyl)but-2-enoate, 6.3 g yellow solid.

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 0.87 (t, $J=7.5$ Hz, 6H), 1.17-1.34 (m, 7H), 1.48-1.62 (m, 4H), 2.51 (s, 3H), 3.16 (t, $J=7.2$ Hz, 4H), 4.18 (q, $J=7.2$ Hz, 2H), 6.14 (d, $J=1.2$ Hz, 1H), 7.53-7.54 (m, 2H), 7.87 (d, $J=2.1$ Hz, 1H).

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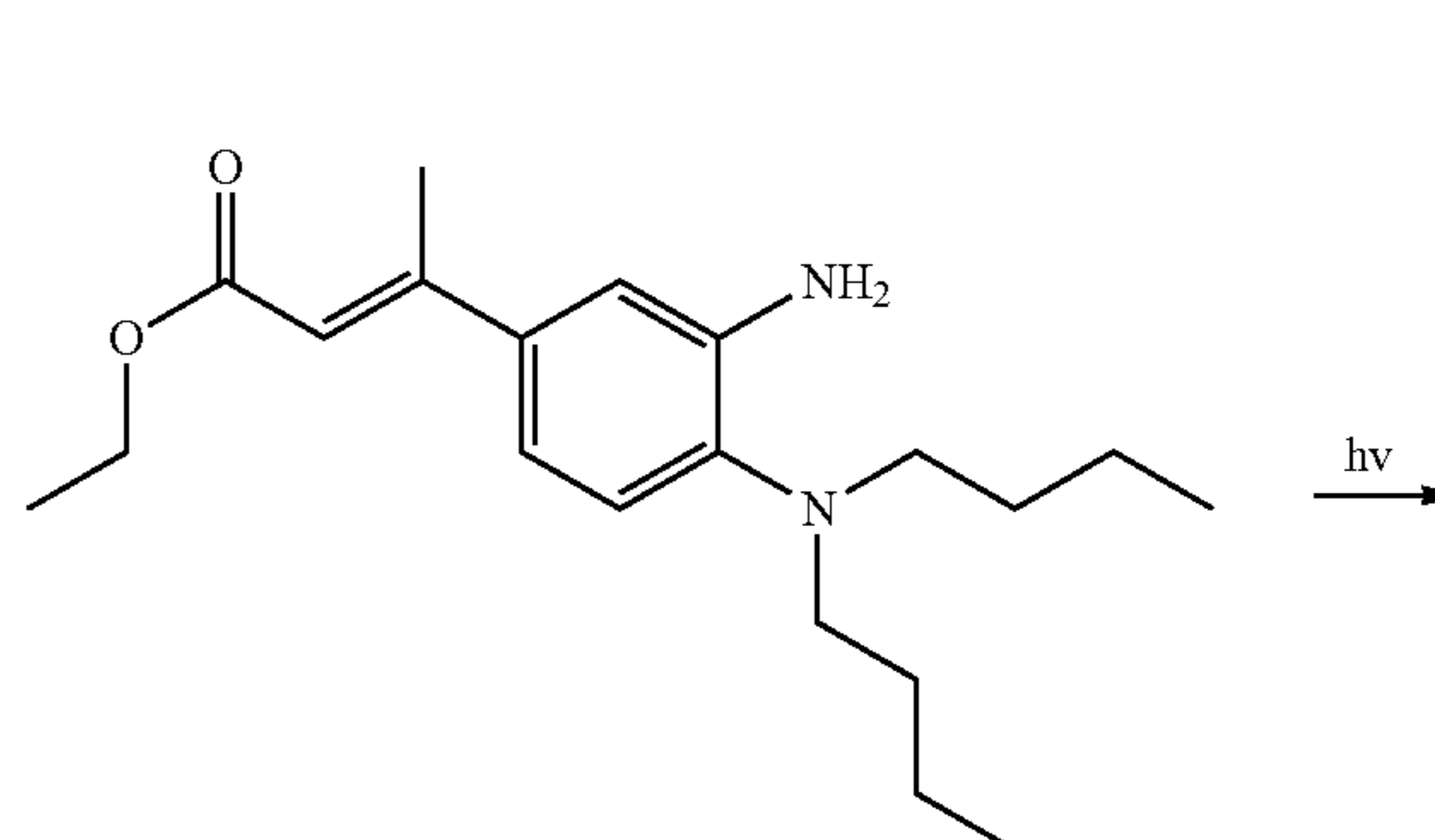
Example 3



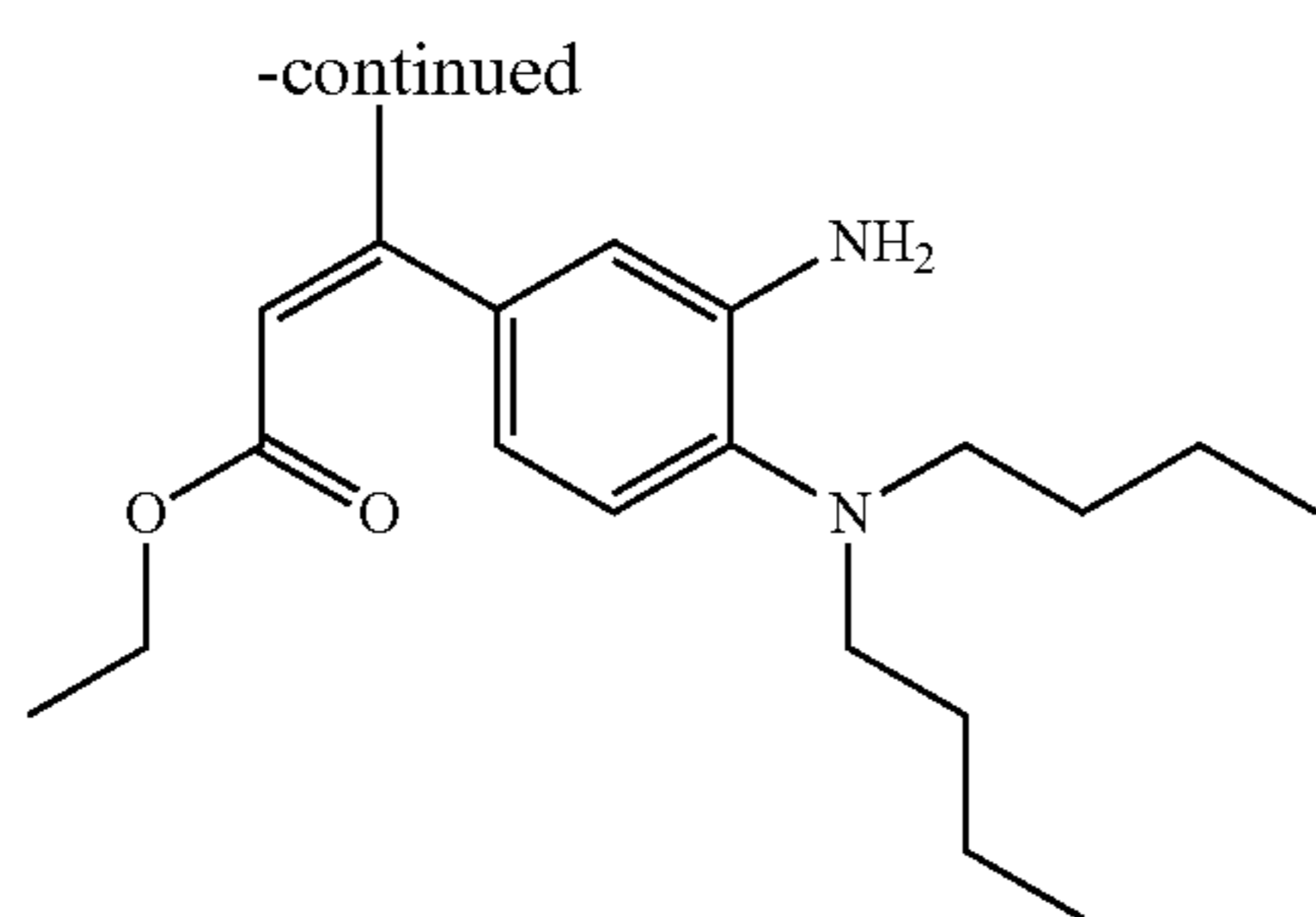
To a 250 mL flask, 2.7 g of compound ethyl (E)-3-(4-(dibutylamino)-3-nitrophenyl)but-2-enoate, 4.0 g of ammonium chloride, zinc powder 4.9 g, 100 mL of ethanol and 20 mL of water were added, the mixture was stirred at room temperature for 2 hours. After reaction was completed by TLC monitoring, the reaction mixture was filtered, and the solvent of filtrate was removed in vacuo. Purification of residues by silica gel column chromatography (eluent ethyl acetate and petroleum ether (boiling range: 60-90° C.), volume ratio: 1:10) to obtain the compound ethyl (E)-3-(3-amino-4-(dibutylamino)phenyl)but-2-enoate, 0.3 g reddish brown viscous liquid.

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ (ppm): 0.87 (t, $J=6.9$ Hz, 6H), 1.10 (t, $J=6.9$ Hz, 3H), 1.23-1.30 (m, 4H), 1.33-1.43 (m, 4H), 2.16 (d, $J=1.5$ Hz, 3H), 2.86 (t, $J=7.5$ Hz, 4H), 4.03 (q, $J=6.9$ Hz, 2H), 6.08 (d, $J=0.9$ Hz, 1H), 6.56-6.60 (m, 2H), 6.96 (d, $J=7.5$ Hz, 1H).

Example 4



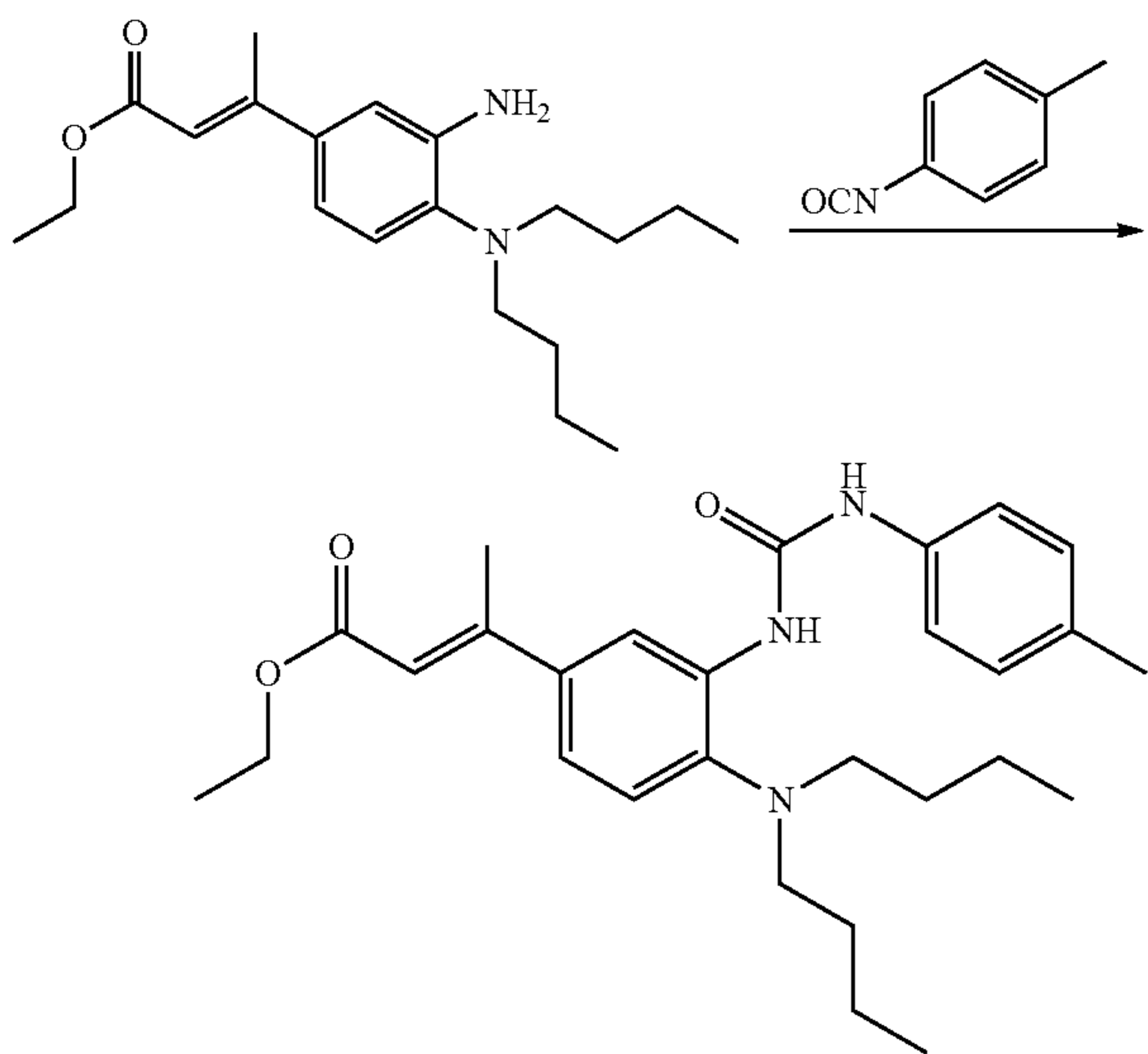
53



To a 100 mL flask, 0.3 g of compound ethyl (E)-3-(3-amino-4-(dibutylamino)phenyl)but-2-enoate and acetonitrile 50 mL were added, irradiated with UV light (wavelength: 365 nm) for 48 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.), volume ratio 1:10) to obtain the compound ethyl (Z)-3-(3-amino-4-(dibutylamino)phenyl)but-2-enoate, 0.11 g reddish brown viscous liquid.

¹H-NMR (300 MHz, CDCl₃) δ (ppm): 0.87 (t, J=6.9 Hz, 6H), 1.09 (t, J=6.9 Hz, 3H), 1.22-1.30 (m, 4H), 1.33-1.42 (m, 4H), 2.15 (d, J=1.5 Hz, 3H), 2.86 (t, J=7.5 Hz, 4H), 4.01 (q, J=6.9 Hz, 2H), 5.82 (d, J=0.9 Hz, 1H), 6.56-6.60 (m, 2H), 6.97 (d, J=7.5 Hz, 1H).

Example 5



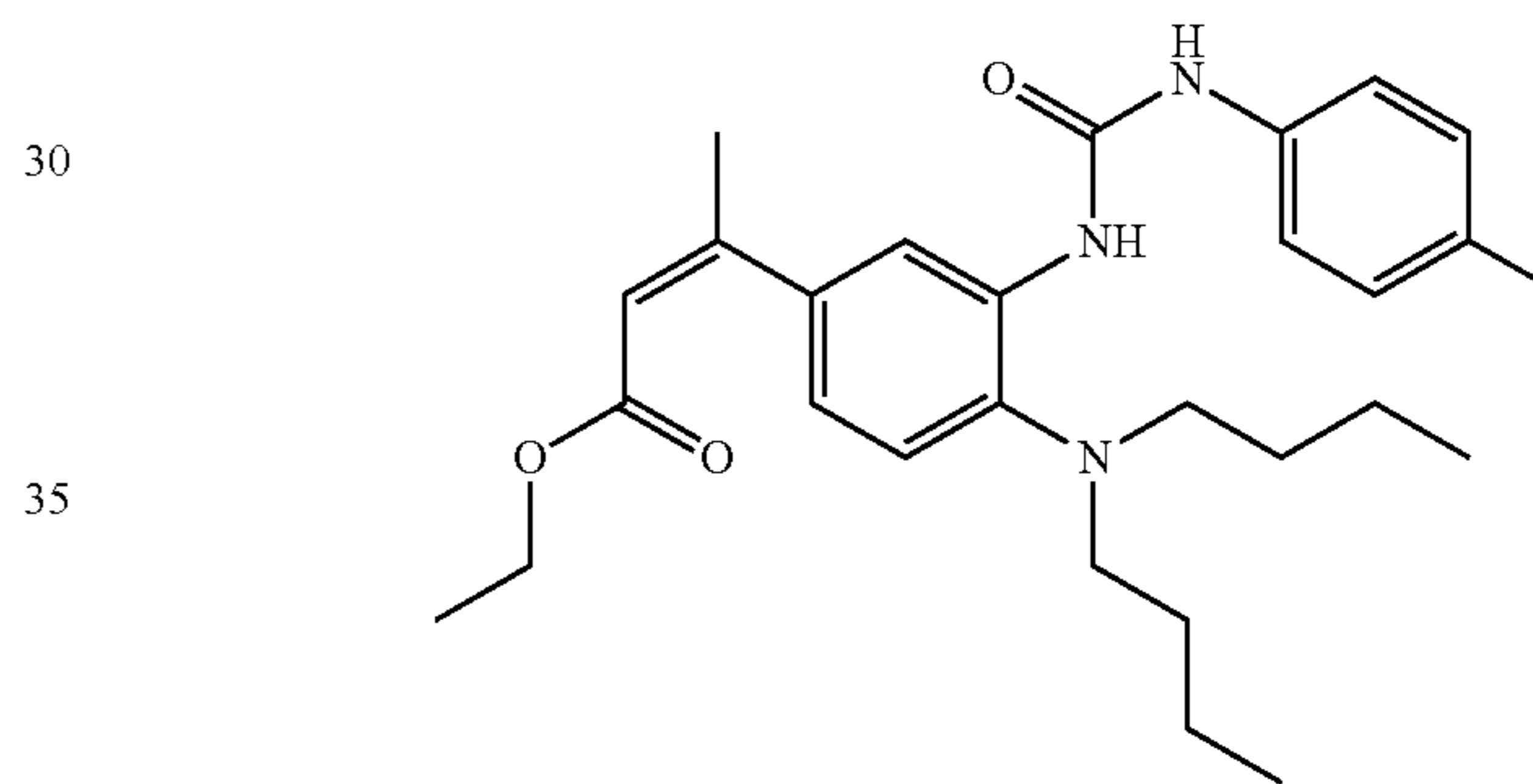
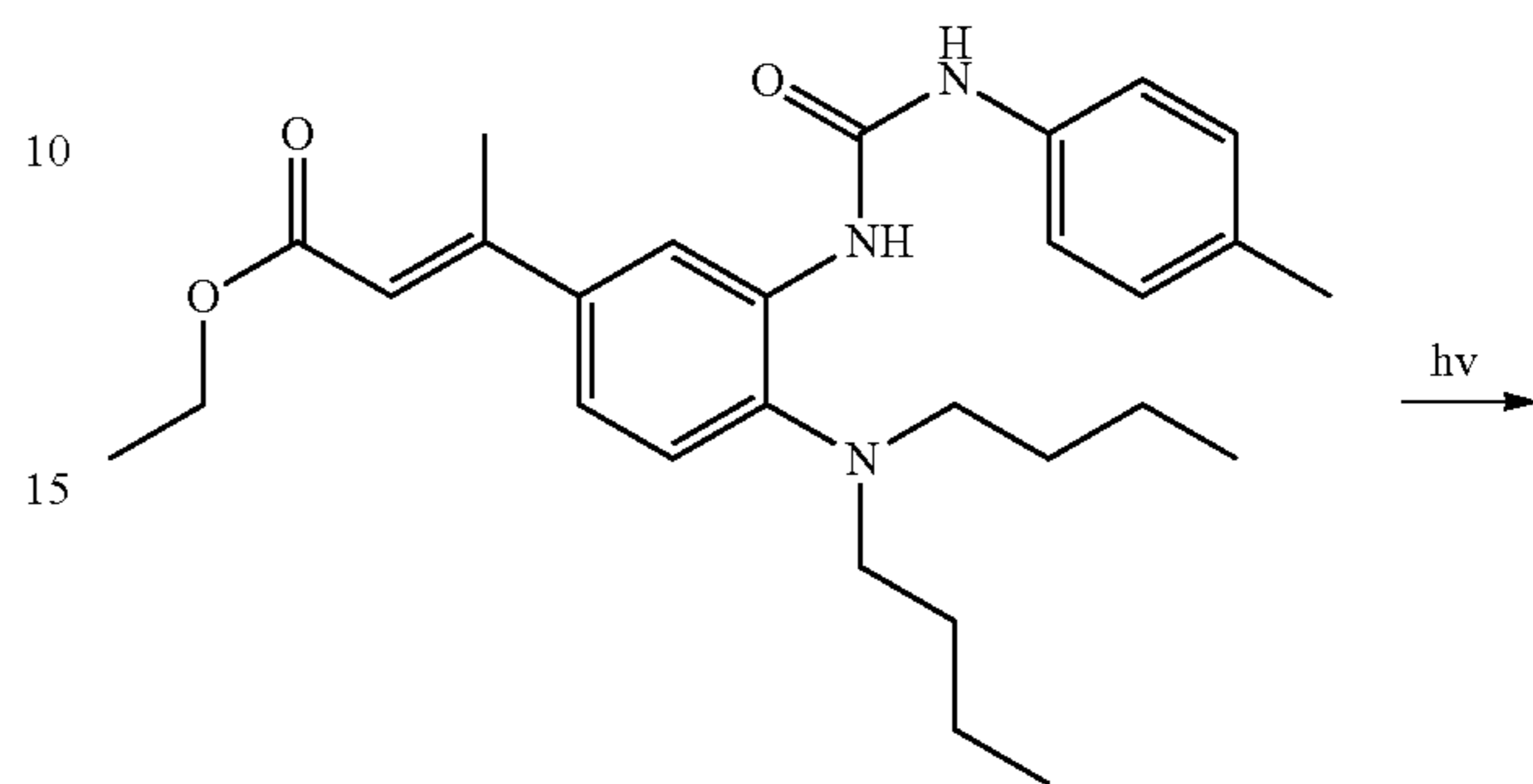
To a 100 mL flask, 0.4 g of the compound ethyl (E)-3-(3-amino-4-(dibutylamino)phenyl)but-2-enoate, 0.16 g of p-toluene isocyanate and 30 mL of tetrahydrofuran were added. The mixture was stirred at room temperature for 8 hours. After reaction was completed by TLC monitoring, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range: 60-90° C.), volume ratio: 1:5) to obtain the compound ethyl (E)-3-(4-(dibutylamino)-3-(p-tolylureido)phenyl)but-2-enoate (Compound 518), 0.12 g white solid.

¹H-NMR (300 MHz, CDCl₃) δ (ppm): 0.81 (t, J=6.9 Hz, 6H), 1.12-1.16 (m, 8H), 1.30 (t, J=6.9 Hz, 3H), 2.35 (s, 3H),

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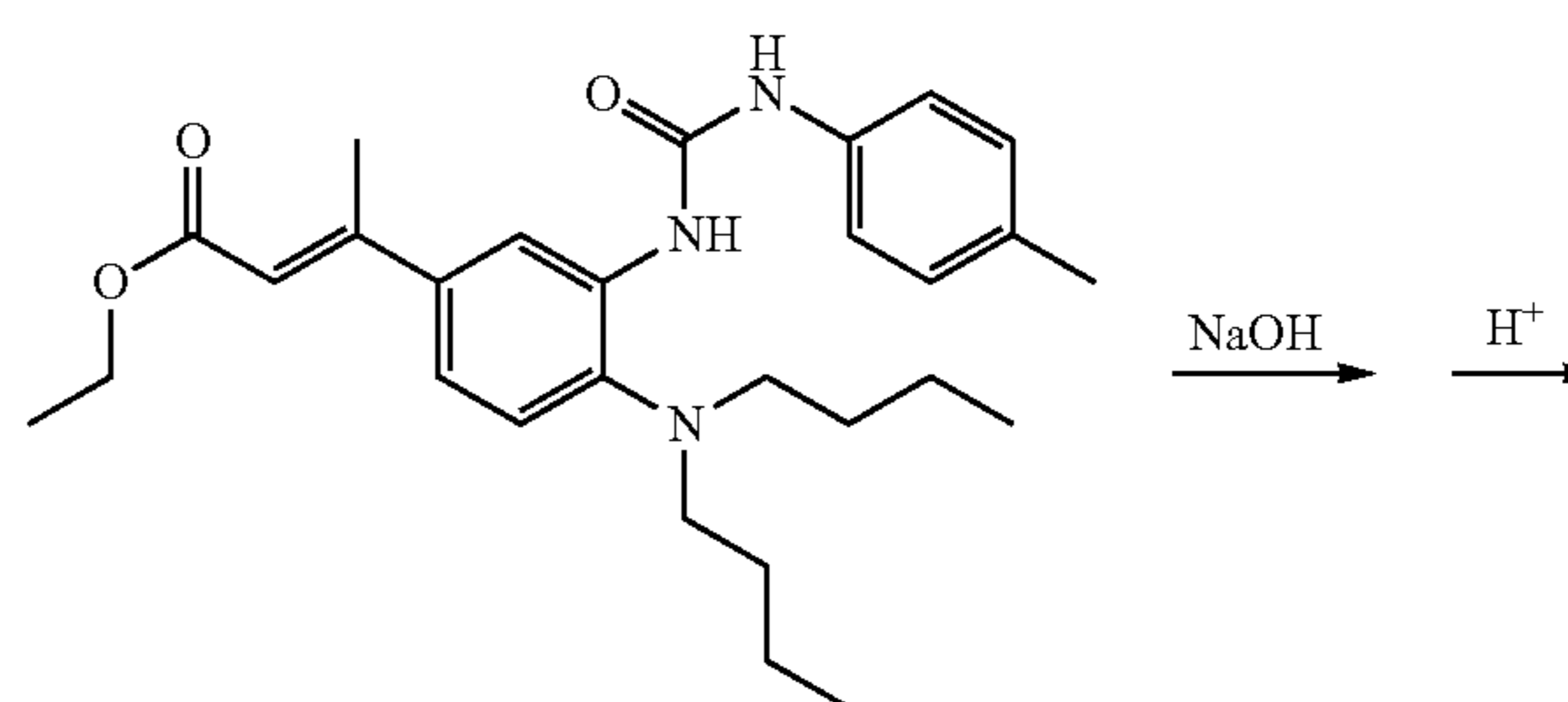
2.72 (t, J=6.9 Hz, 4H), 4.18 (q, J=6.9 Hz, 2H), 6.18 (s, 1H), 6.45 (s, 1H), 7.08-7.26 (m, 5H), 8.22 (s, 1H), 8.45 (s, 1H).

Example 6



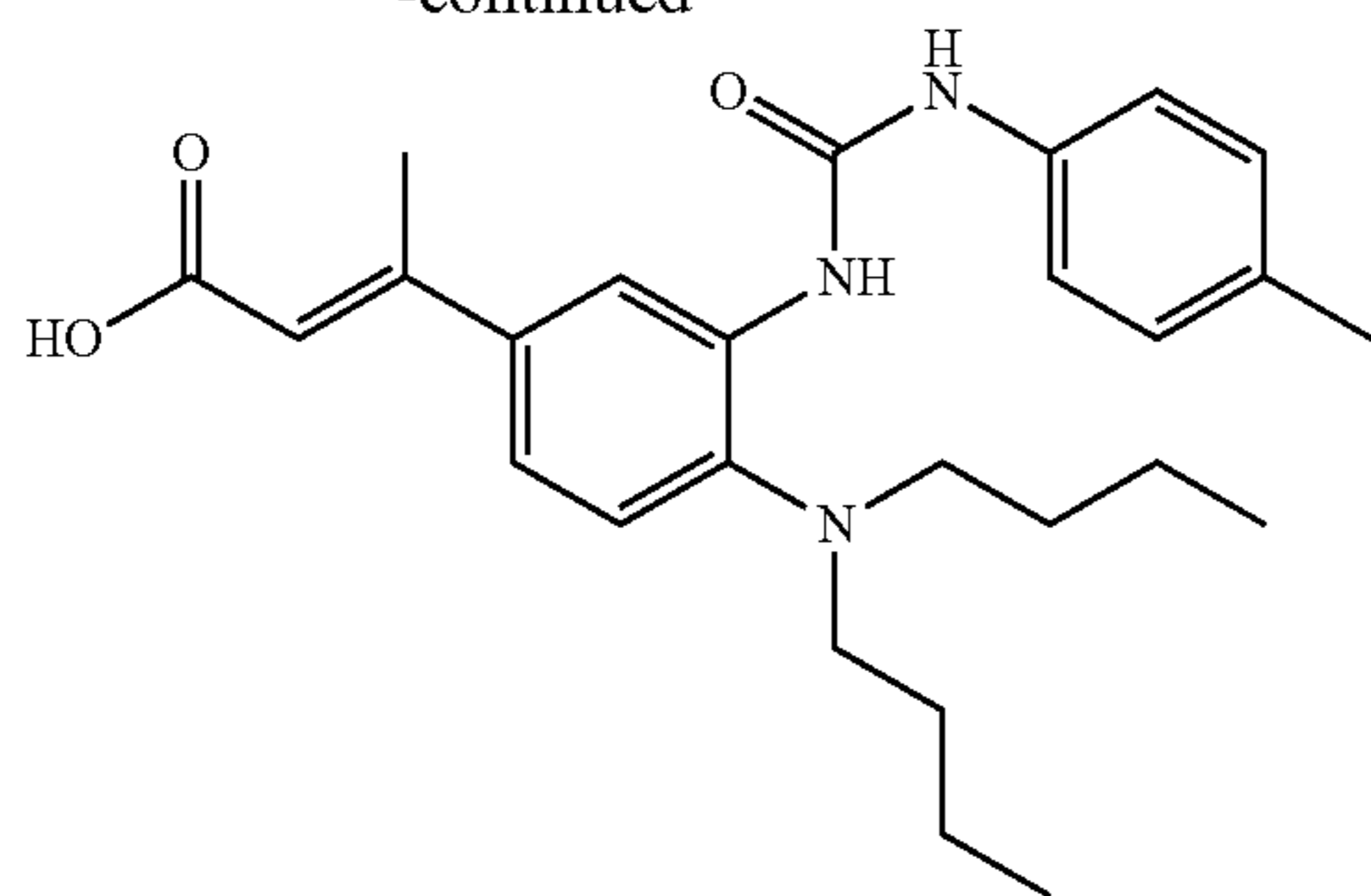
To a 100 mL flask, 0.3 g of the compound ethyl (E)-3-(4-(dibutylamino)-3-(p-tolylureido)phenyl)but-2-enoate and acetonitrile 50 mL were added, irradiated with UV light (wavelength: 365 nm) for 48 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.), volume ratio 1:6) to obtain the compound ethyl (Z)-3-(4-(dibutylamino)-3-(p-tolylureido)phenyl)but-2-enoate (Compound 2), 0.10 g white solid.

Example 7



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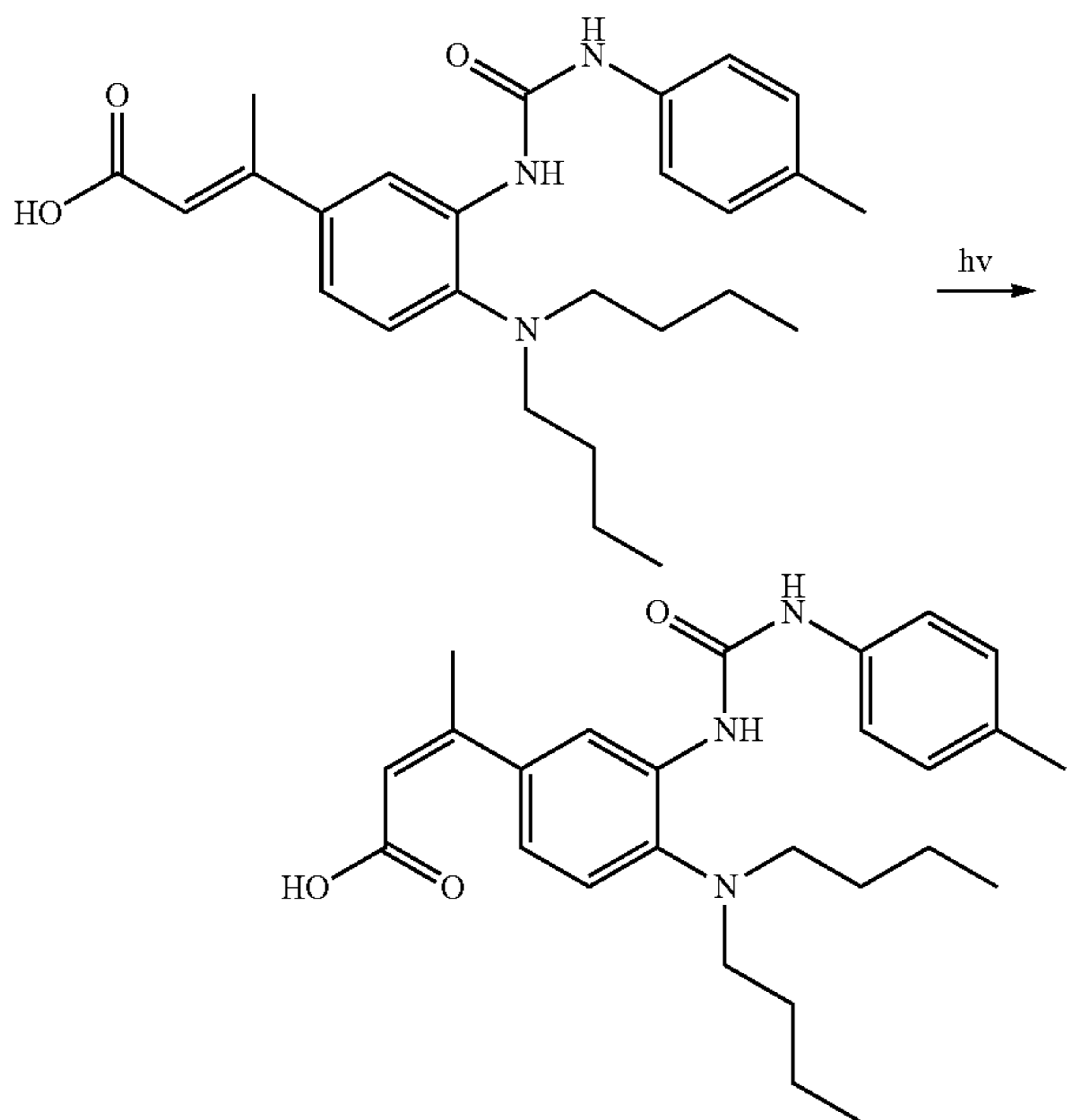
-continued



To a 100 mL flask, 100 g of compound ethyl (E)-3-(4-(diethylamino)-3-(3-(p-tolyl)ureido)phenyl)but-2-enoate, ethanol 50 mL and 3.0 g of sodium hydroxide were added. The mixture was stirred at room temperature for 12 hours. After reaction was completed by TLC monitoring, the solvent was removed in vacuo, and the residue was dissolved in ethyl acetate (300 mL) and water (100 mL), and the mixture was adjusted to pH=3 with concentrated hydrochloric acid, and the organic phase was dried over anhydrous sodium sulfate for 12 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.) in a volume ratio of 1:2) to obtain the compound (E)-3-(4-(diethylamino)-3-(3-(p-tolyl)ureido)phenyl)but-2-enoic acid (Compound 525), 0.11 g white solid.

¹H-NMR (300 MHz, CDCl₃) δ (ppm): 0.81 (t, J=6.9 Hz, 6H), 1.13-1.17 (m, 8H), 2.35 (s, 3H), 2.73 (t, J=6.9 Hz, 4H), 6.17 (s, 1H), 6.46 (s, 1H), 7.07-7.25 (m, 5H), 8.23 (s, 1H), 8.46 (s, 1H), 12.05 (s, 1H). MS (ESI), m/z (%): 438.32 [M+H]⁺.

Example 8

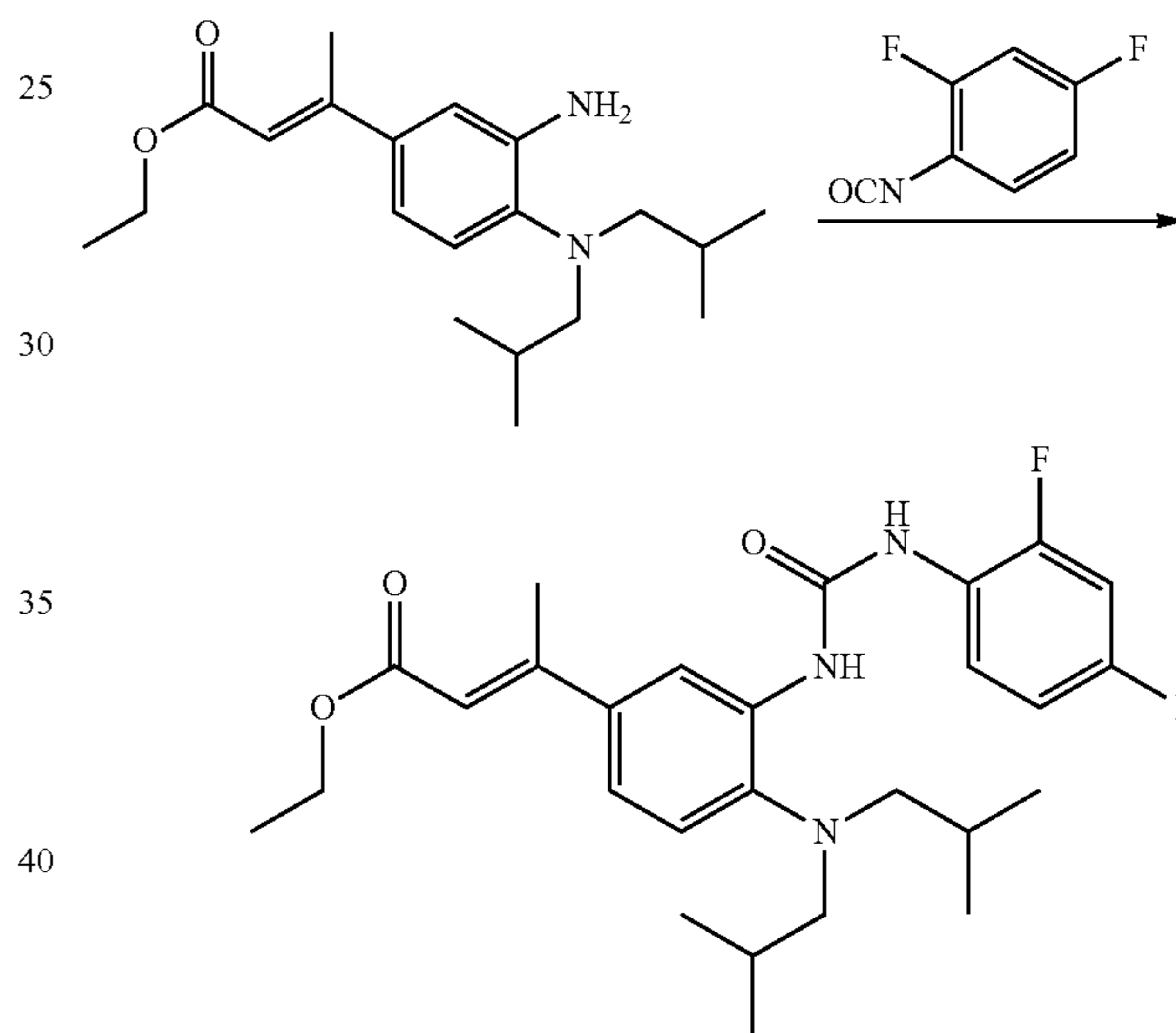


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To a 100 mL flask, 0.3 g of compound (E)-3-(4-(diethylamino)-3-(3-(p-tolyl)ureido)phenyl)but-2-enoic acid and 50 mL of acetonitrile were added, irradiated with UV light (wavelength: 365 nm) for 48 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.), volume ratio 1:2) to obtain compound (Z)-3-(4-(diethylamino)-3-(3-(p-tolyl)ureido)phenyl)but-2-enoic acid (Compound 9), 0.16 g white solid.

¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.19-1.31 (m, 8H), 2.26 (s, 3H), 2.50 (s, 3H), 2.83-2.88 (m, 4H), 5.81 (s, 1H), 7.03-7.12 (m, 3H), 7.33-7.37 (m, 2H), 8.04 (s, 1H), 8.82-8.36 (m, 1H), 8.36 (s, 1H), 9.35 (s, 1H). MS (ESI), m/z (%): 438.32 [M+H]⁺.

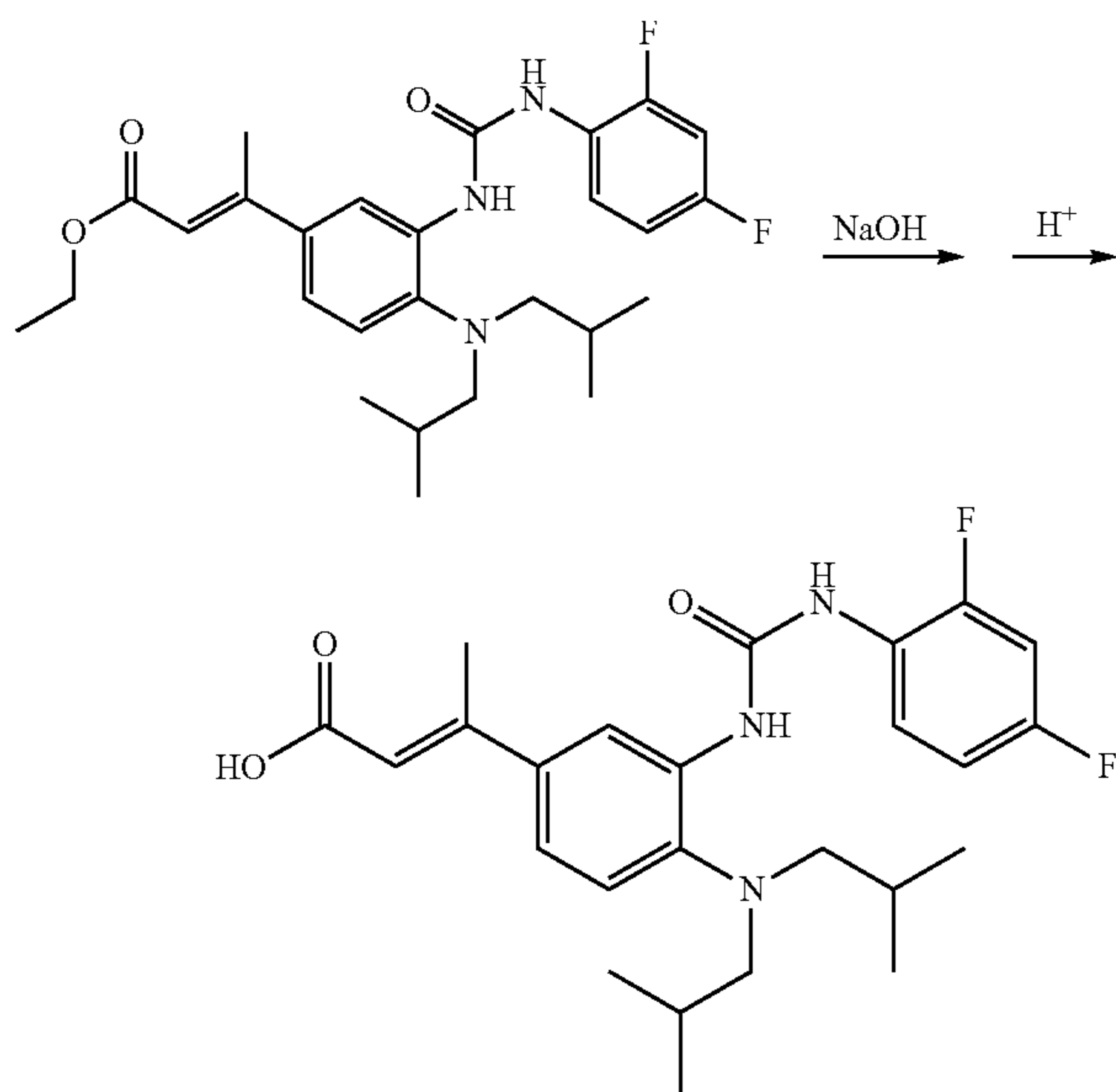
Example 9



To a 100 mL flask, 0.5 g of the compound ethyl (E)-3-(3-amino-4-(diisobutylamino)phenyl)but-2-enoate (preparation method is the same as in Example 1, Example 2 and Example 3), 3 g of 2,4-difluorophenyl isocyanate and 30 mL of tetrahydrofuran were added. The mixture was stirred at room temperature for 4 hours. After reaction was completed by TLC monitoring, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range: 60-90° C.), volume ratio: 1:5) to obtain the compound ethyl (E)-3-(3-(2,4-difluorophenyl)ureido)-4-(diisobutylamino)phenyl)but-2-enoate (Compound 564), 0.16 g white solid.

¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.83 (d, J=6.0 Hz, 12H), 1.24 (t, J=6.0 Hz, 3H), 1.69-1.72 (m, 2H), 2.49 (s, 3H), 2.79 (d, J=12.0 Hz, 4H), 4.13 (q, J=6.0 Hz, 2H), 6.09 (s, 1H), 7.03-7.05 (m, 1H), 7.19-7.23 (m, 2H), 7.29-7.31 (t, J=6 Hz, 1H), 7.98-8.01 (m, 1H), 8.05 (d, J=6.0 Hz, 1H), 8.09 (s, 1H), 9.33 (s, 1H). MS (ESI), m/z (%): 488.32[M+H]⁺.

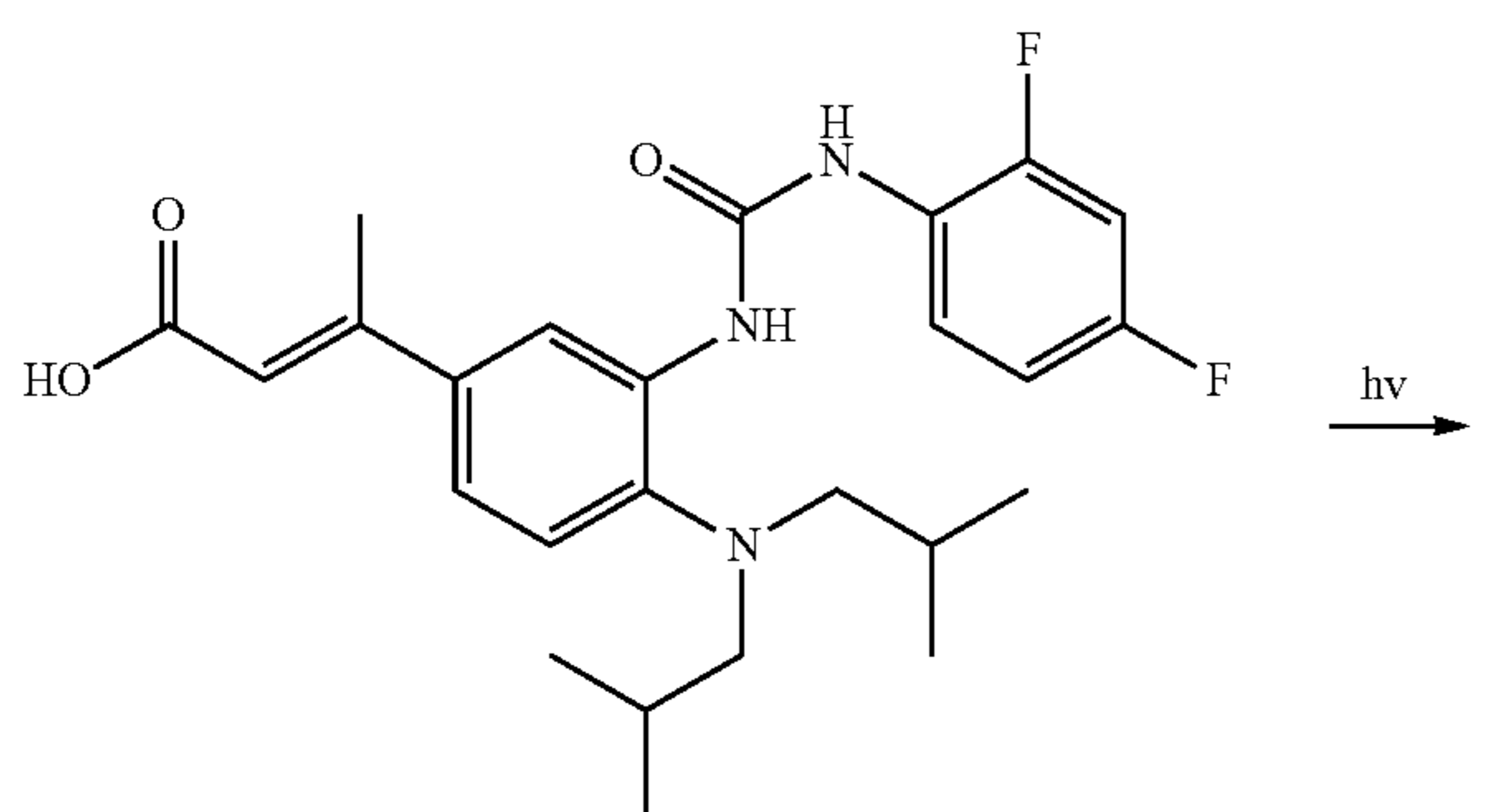
57
Example 10



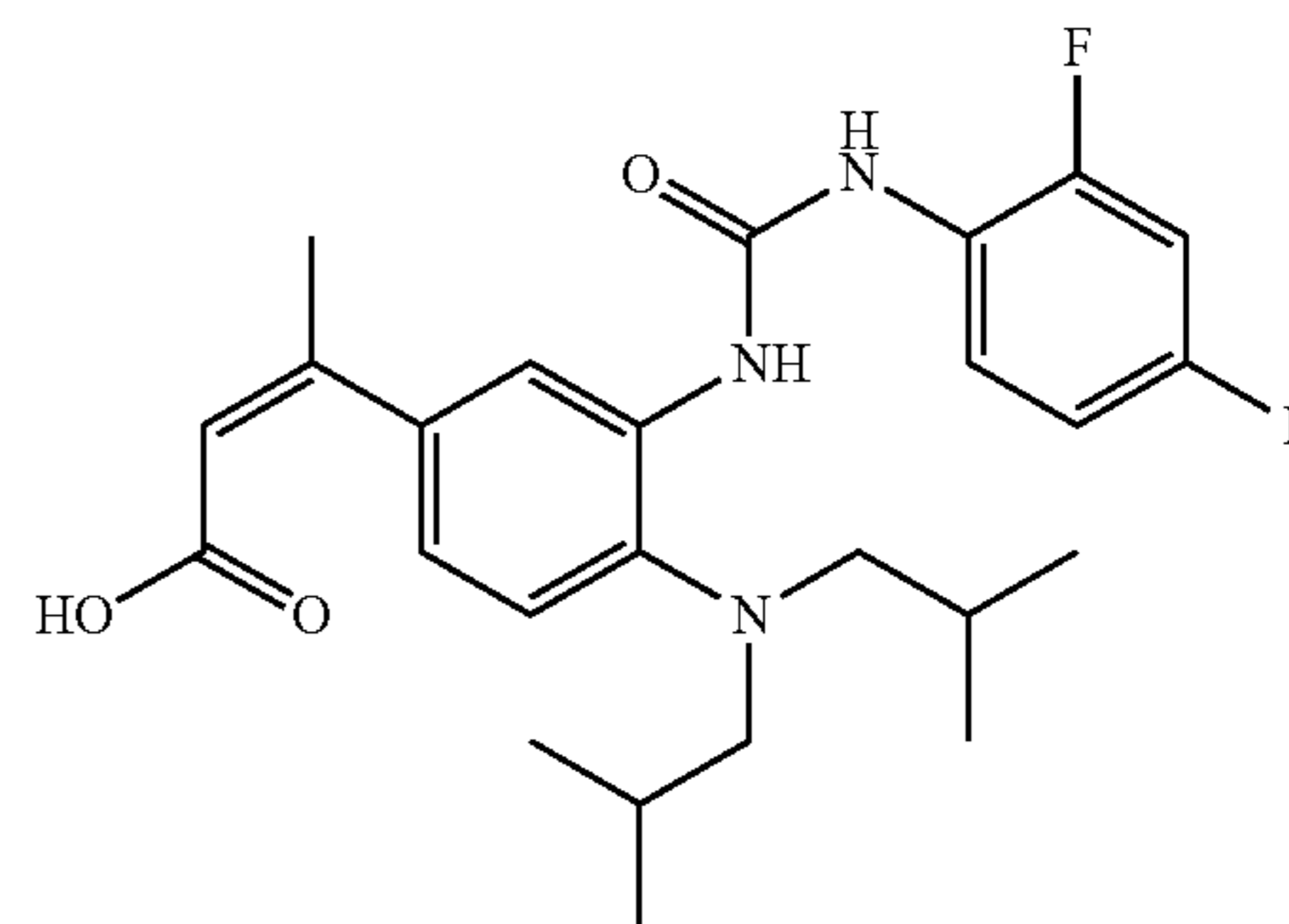
To a 100 mL flask, 0.3 g of the compound ethyl (E)-3-(3-(3-(2,4-difluorophenyl)ureido)-4-(diisobutylamino)phenyl)but-2-enoate, ethanol 50 mL and sodium hydroxide 3.0 g were added. The mixture was stirred at room temperature for 12 hours. After reaction was completed by TLC monitoring, the solvent was removed in vacuo, and the residue was dissolved in ethyl acetate (300 mL) and water (100 mL), and the mixture was adjusted to pH=3 with concentrated hydrochloric acid, and the organic phase was dried over anhydrous sodium sulfate for 12 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.), volume ratio 1:2) to obtain the compound (E)-3-(3-(3-(2,4-difluorophenyl)ureido)-4-(diisobutylamino)phenyl)but-2-enoic acid (Compound 57), 0.15 g white solid.

¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 9.31 (s, 1H), 8.08 (s, 1H), 8.05 (d, J=6.0 Hz, 1H), 7.98-8.03 (m, 1H), 7.29-7.31 (t, J=6 Hz, 1H), 7.19-7.24 (m, 2H), 7.01-7.06 (m, 1H), 6.05 (s, 1H), 2.86-2.90 (m, 4H), 2.48 (s, 3H), 1.69-1.72 (m, 2H), 0.82 (d, J=6.0 Hz, 12H). MS (ESI), m/z (%): 460.27[M+H]⁺.

Example 11



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-continued

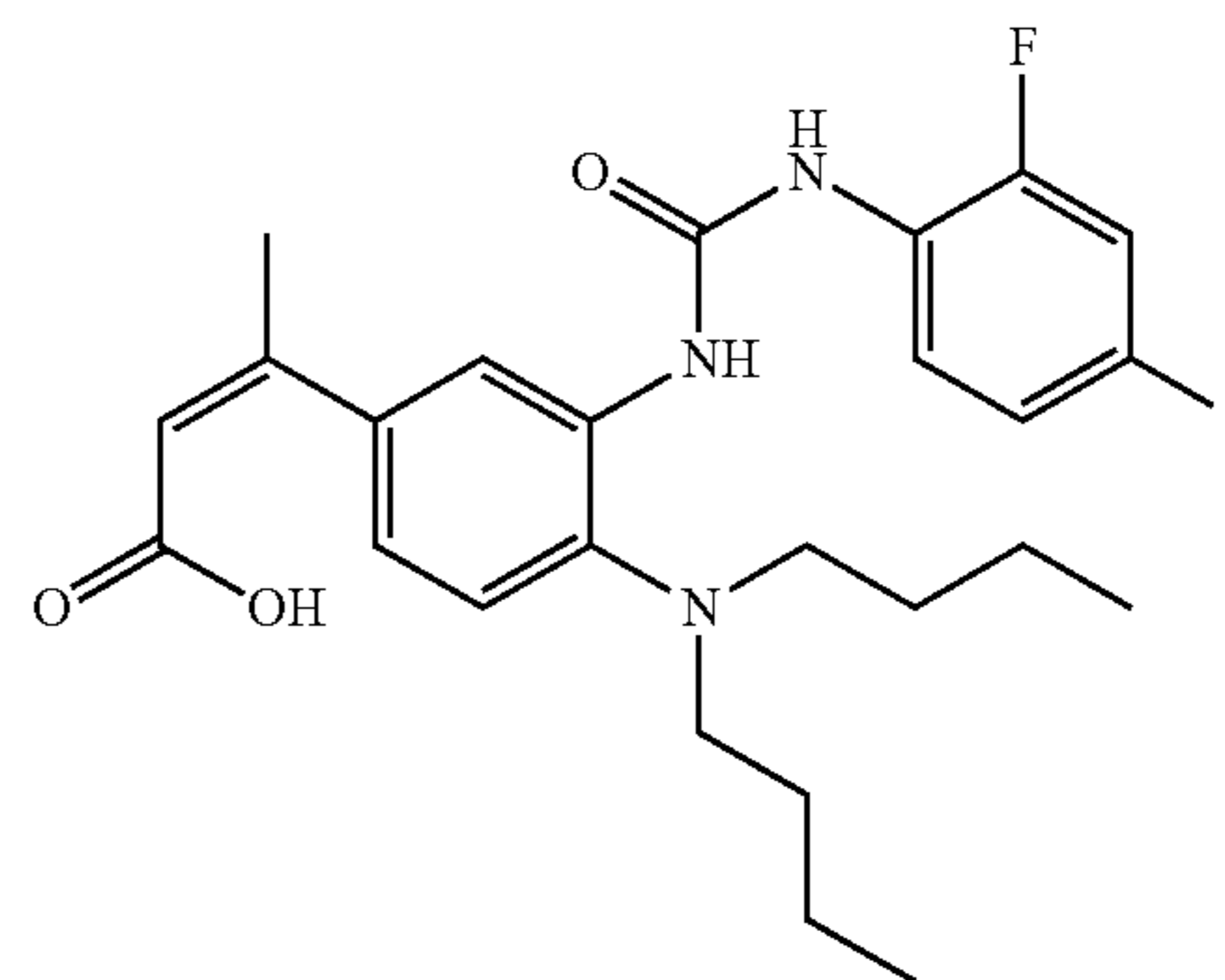


To a 100 mL flask, 0.1 g of compound (E)-3-(3-(3-(2,4-difluorophenyl)ureido)-4-(diisobutylamino)phenyl)but-2-enoic acid and 50 mL of acetonitrile, irradiated with UV light (wavelength: 365 nm) for 48 hours, the solvent was removed in vacuo. Purification of residues by silica gel column chromatography (eluent is ethyl acetate and petroleum ether (boiling range 60-90° C.), volume ratio 1:2) to obtain the compound (Z)-3-(3-(3-(2,4-difluorophenyl)ureido)-4-(diisobutylamino)phenyl)but-2-enoic acid (Compound 58), 0.03 g white solid.

¹H-NMR (600 MHz, DMSO-d₆) δ 11.88 (s, 1H), 9.28 (s, 1H), 8.05 (s, 1H), 7.94 (td, J=9.1, 6.5 Hz, 1H), 7.78 (d, J=1.7 Hz, 1H), 7.34-7.24 (m, 1H), 7.13 (d, J=8.3 Hz, 1H), 7.04 (t, J=8.0 Hz, 1H), 6.87 (dd, J=8.2, 1.6 Hz, 1H), 5.84 (s, 1H), 2.70 (d, J=6.8 Hz, 4H), 2.09 (s, 3H), 1.71-1.66 (m, 2H), 0.85 (d, J=6.0 Hz, 12H). MS (ESI), m/z (%): 460.28[M+H]⁺.

Partial Compound Nuclear Magnetic Resonance Data:

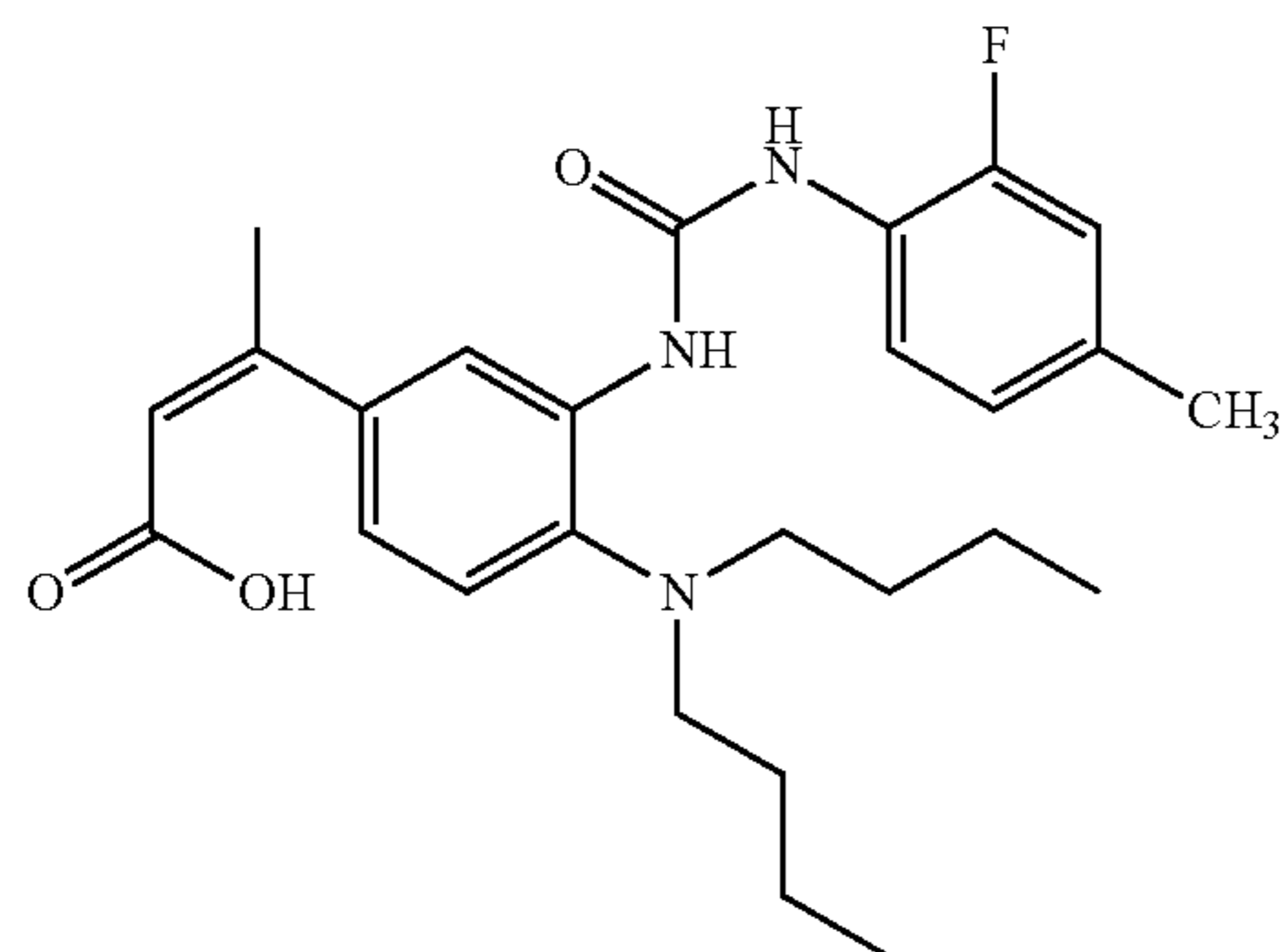
Compound 13



¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.45-1.17 (m, 8H), 2.50 (s, 3H), 2.87 (m, 4H), 5.86 (s, 1H), 6.85-7.32 (m, 4H), 8.05-8.00 (m, 1H), 8.25-8.32 (m, 1H), 8.66 (s, 1H), 9.40 (s, 1H). MS (ESI), m/z (%): 460.29 [M+H]⁺. White solid.

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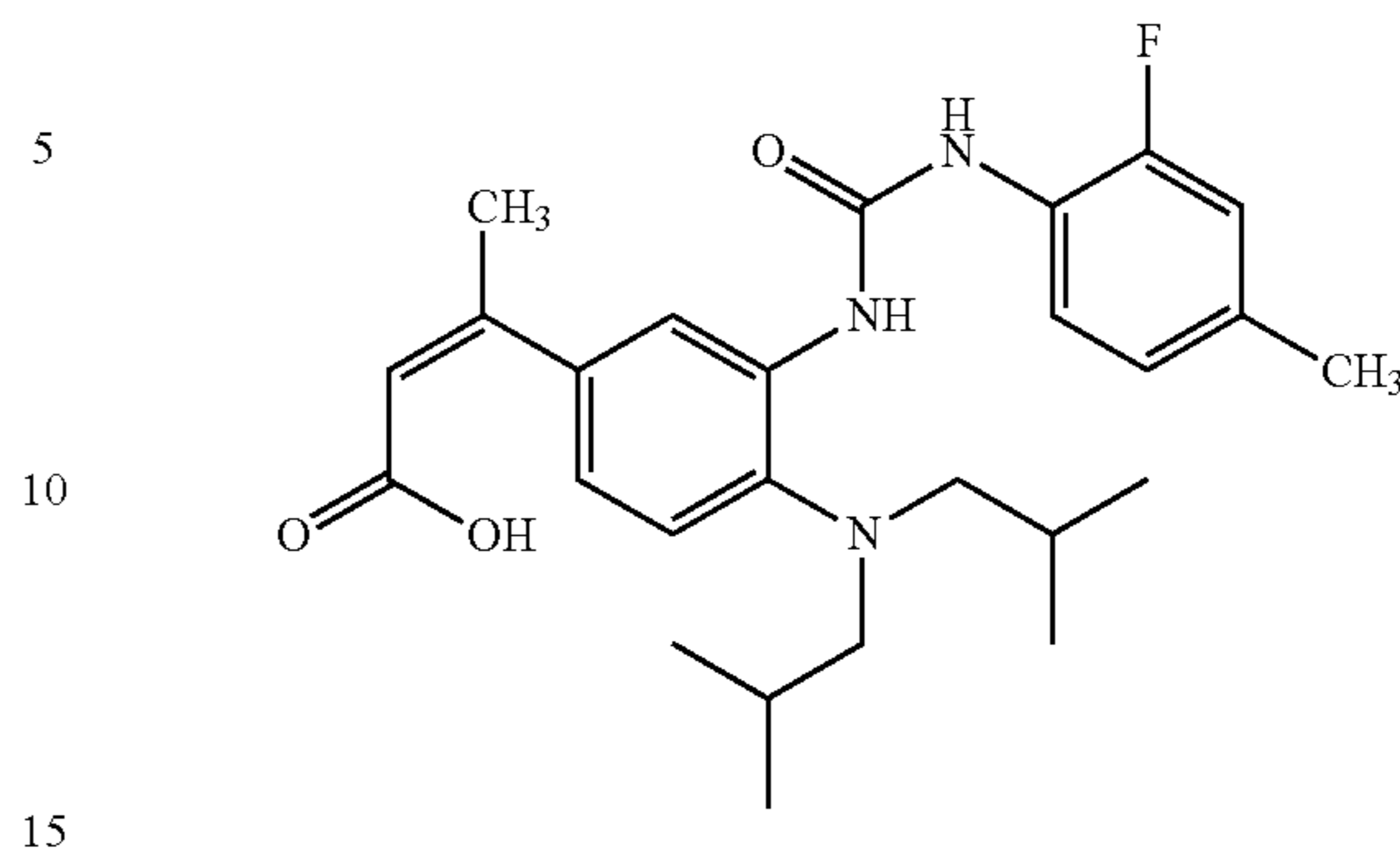
Compound 14



¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.0 Hz, 6H), 1.17-1.37 (m, 8H), 2.27 (s, 3H), 2.50 (s, 3H), 2.86-2.90 (m, 4H), 5.85 (s, 1H), 6.83 (d, J=0.6 Hz, 1H), 6.95 (d, J=0.6 Hz, 1H), 7.06 (d, J=1.2 Hz, 1H), 7.16 (dd, J=4.2, 1.2 Hz, 1H), 7.88-7.94 (m, 1H), 8.33 (s, 1H), 8.63 (s, 1H), 9.28 (s, 1H). MS (ESI), m/z (%): 456.32[M+H]⁺. White solid.

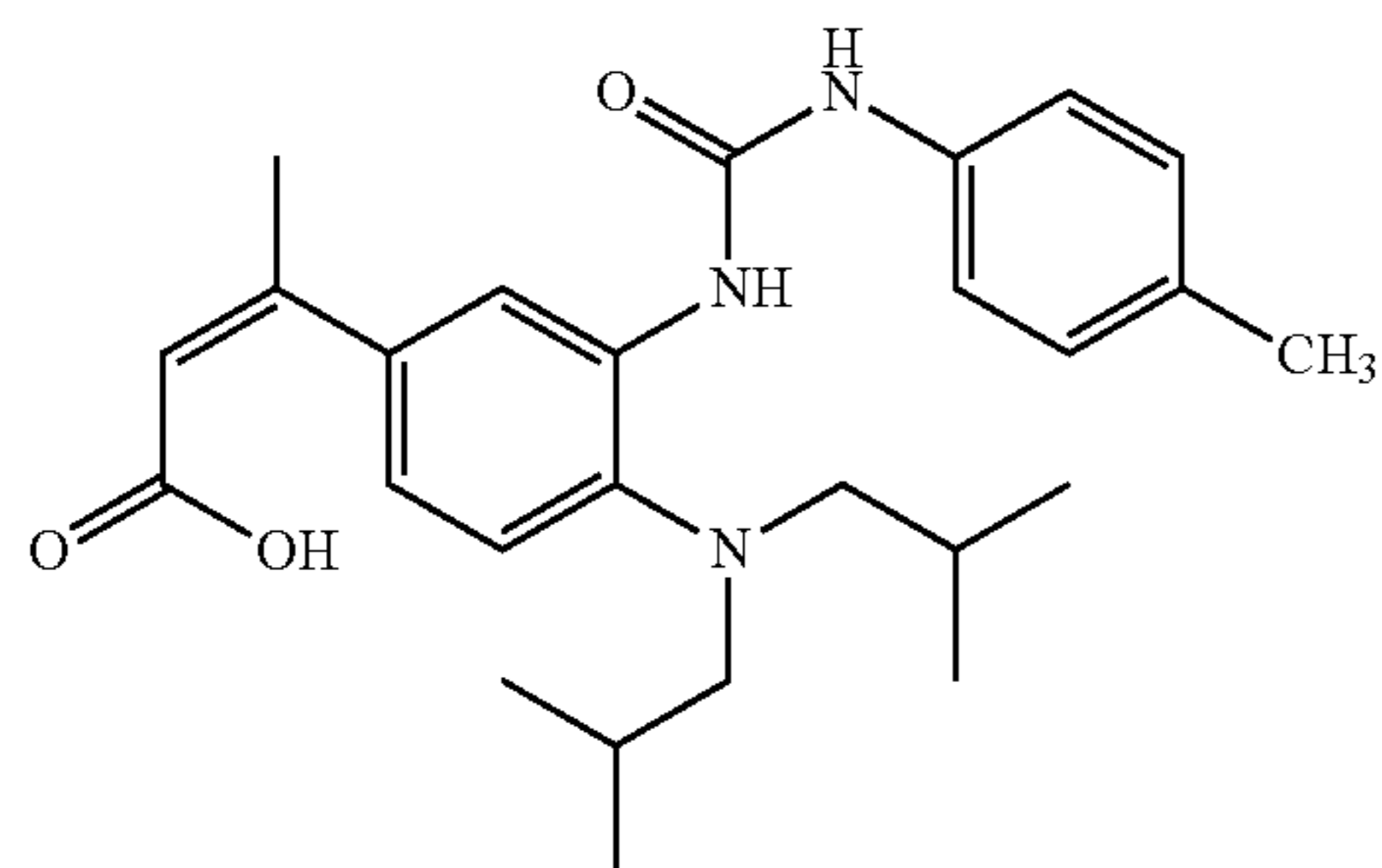
60

Compound 56



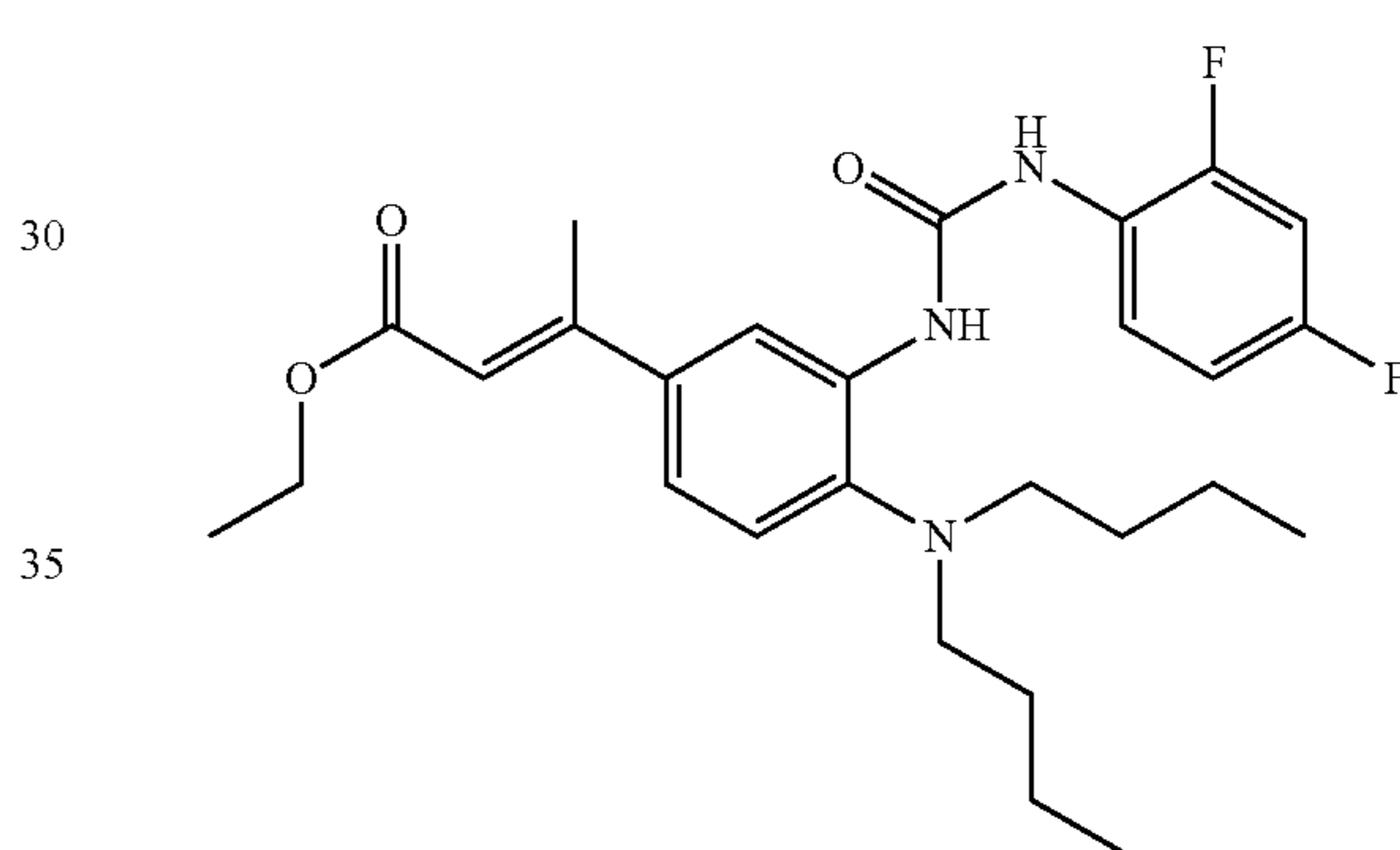
¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 9.28 (s, 1H), 8.63 (s, 1H), 8.33 (s, 1H), 7.88-7.94 (m, 1H), 7.16 (dd, J=4.2, 1.2 Hz, 1H), 7.06 (d, J=1.2 Hz, 1H), 6.95 (d, J=0.6 Hz, 1H), 6.83 (d, J=0.6 Hz, 1H), 5.85 (s, 1H), 2.86-2.90 (m, 4H), 2.48 (s, 3H), 2.10 (s, 3H), 1.63-1.71 (m, 2H), 0.82 (d, J=6.0 Hz, 12H). MS (ESI), m/z (%): 456.29[M+H]⁺. White solid.

Compound 51



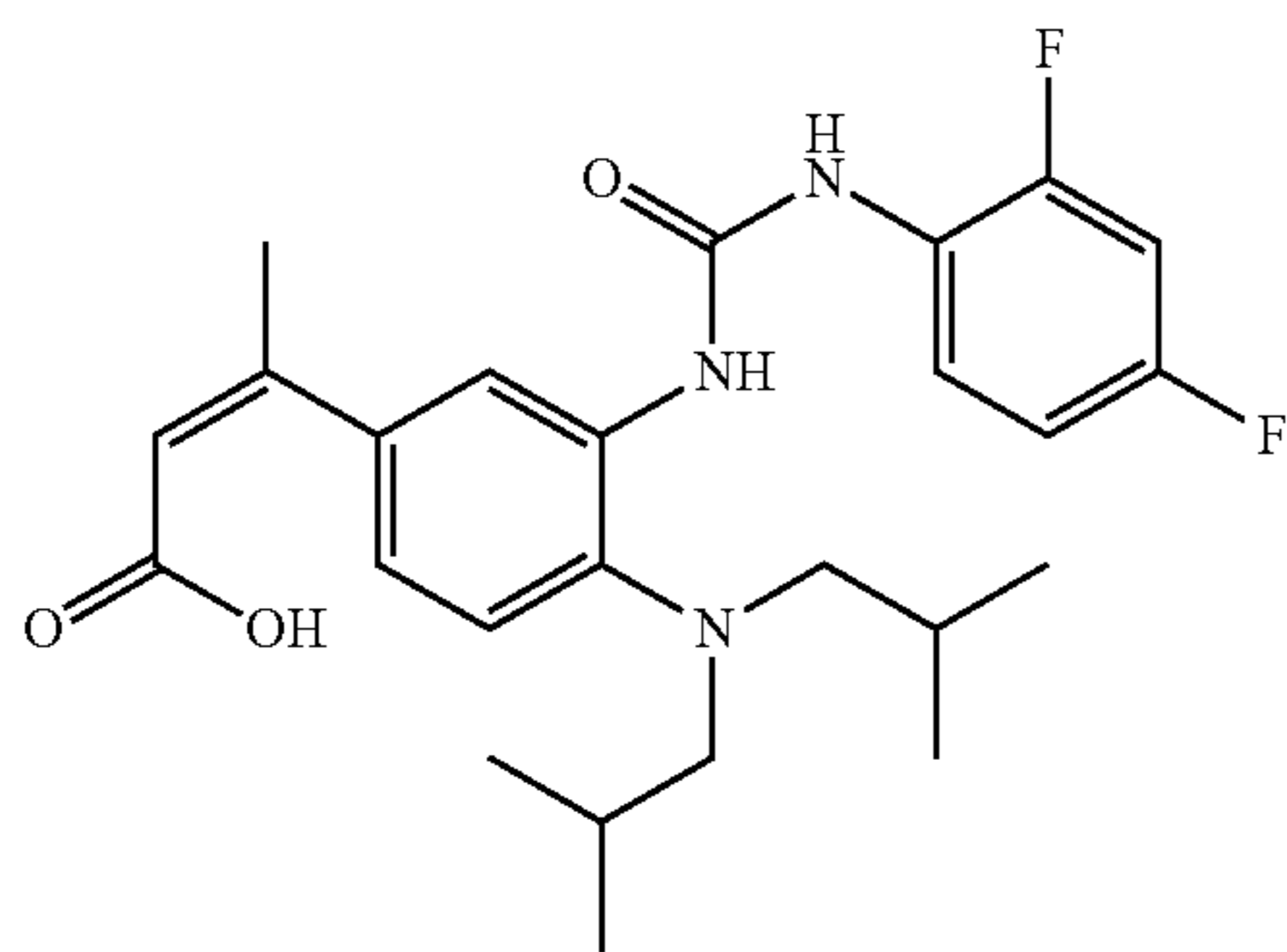
¹H-NMR (600 MHz, DMSO-d₆) δ 12.21 (s, 1H), 9.22 (s, 1H), 8.06 (s, 1H), 8.00 (s, 1H), 7.86 (t, J=8.5 Hz, 1H), 7.45 (d, J=15.8 Hz, 1H), 7.28 (d, J=9.6 Hz, 1H), 7.16 (d, J=8.4 Hz, 1H), 7.05 (d, J=12.2 Hz, 1H), 6.92 (d, J=8.0 Hz, 1H), 5.89 (s, 1H), 2.80 (d, J=6.9 Hz, 4H), 2.45 (d, J=0.7 Hz, 3H), 2.21 (s, 3H), 1.71 (dt, J=13.3, 6.7 Hz, 2H), 0.82 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 438.30[M+H]⁺. White solid.

Compound 396



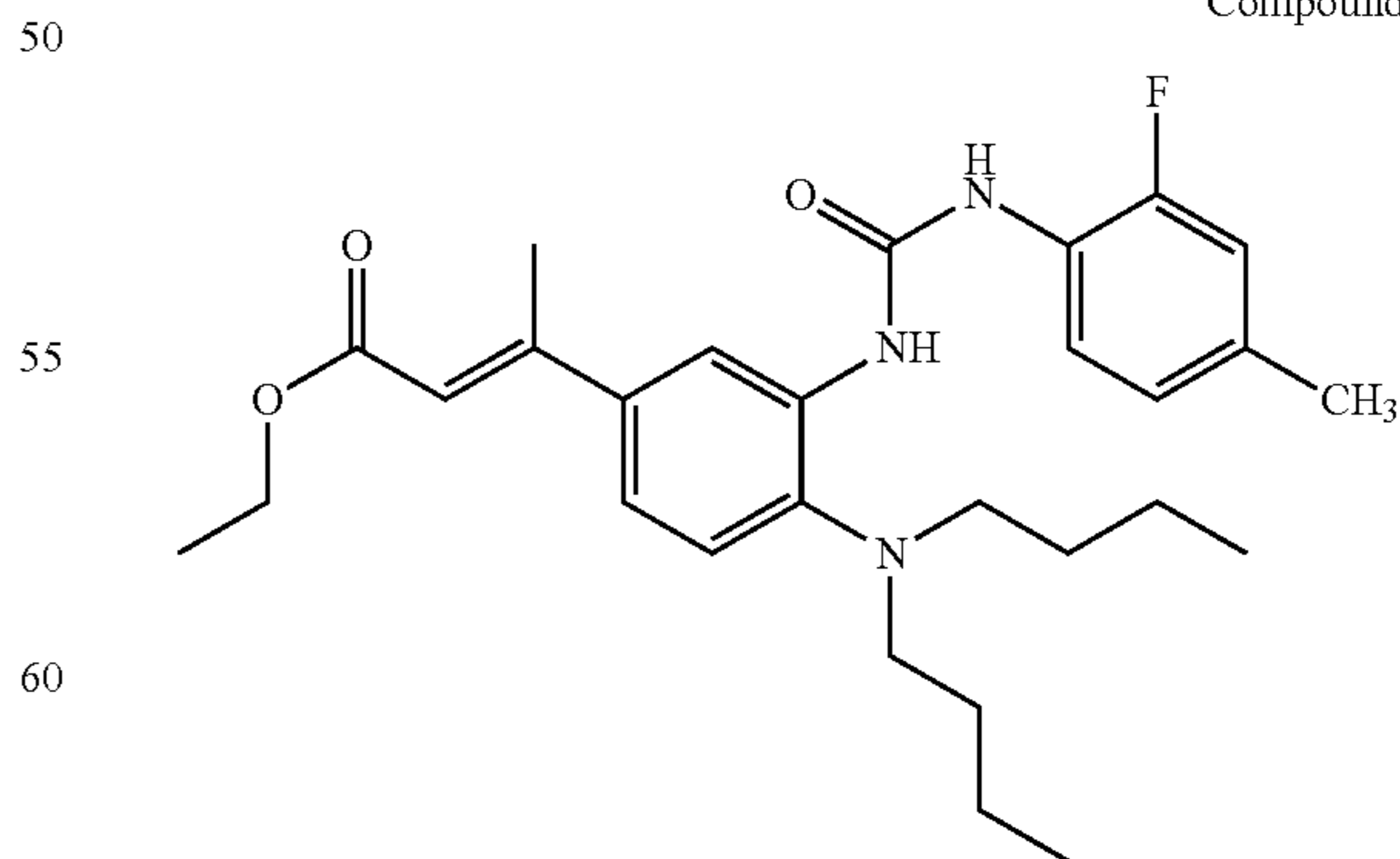
¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.27-1.30 (m, 11H), 2.53 (s, 3H), 2.87-2.89 (m, 4H), 4.13 (q, J=6.9 Hz, 2H), 6.08 (s, 1H), 7.13-7.17 (m, 2H), 7.50 (d, J=9.3 Hz, 1H), 7.70 (d, J=9.3 Hz, 1H), 8.01 (s, 1H), 8.35 (s, 1H), 8.39 (s, 1H), 9.88 (s, 1H). MS (ESI), m/z (%): 488.55[M+H]⁺. White solid.

Compound 55



¹H-NMR (600 MHz, DMSO-d₆) δ 11.88 (s, OH), 9.28 (s, OH), 8.05 (s, 1H), 7.94 (td, J=9.1, 6.5 Hz, 1H), 7.78 (d, J=1.7 Hz, 1H), 7.34-7.24 (m, 1H), 7.13 (d, J=8.3 Hz, 1H), 7.04 (t, J=8.0 Hz, 1H), 6.87 (dd, J=8.2, 1.6 Hz, 1H), 5.84 (s, 1H), 2.70 (d, J=6.8 Hz, 4H), 2.09 (s, 3H), 1.71-1.66 (m, 2H), 0.85 (t, J=8.0 Hz, 12H). MS (ESI), m/z (%): 460.28[M+H]⁺. White solid.

Compound 397

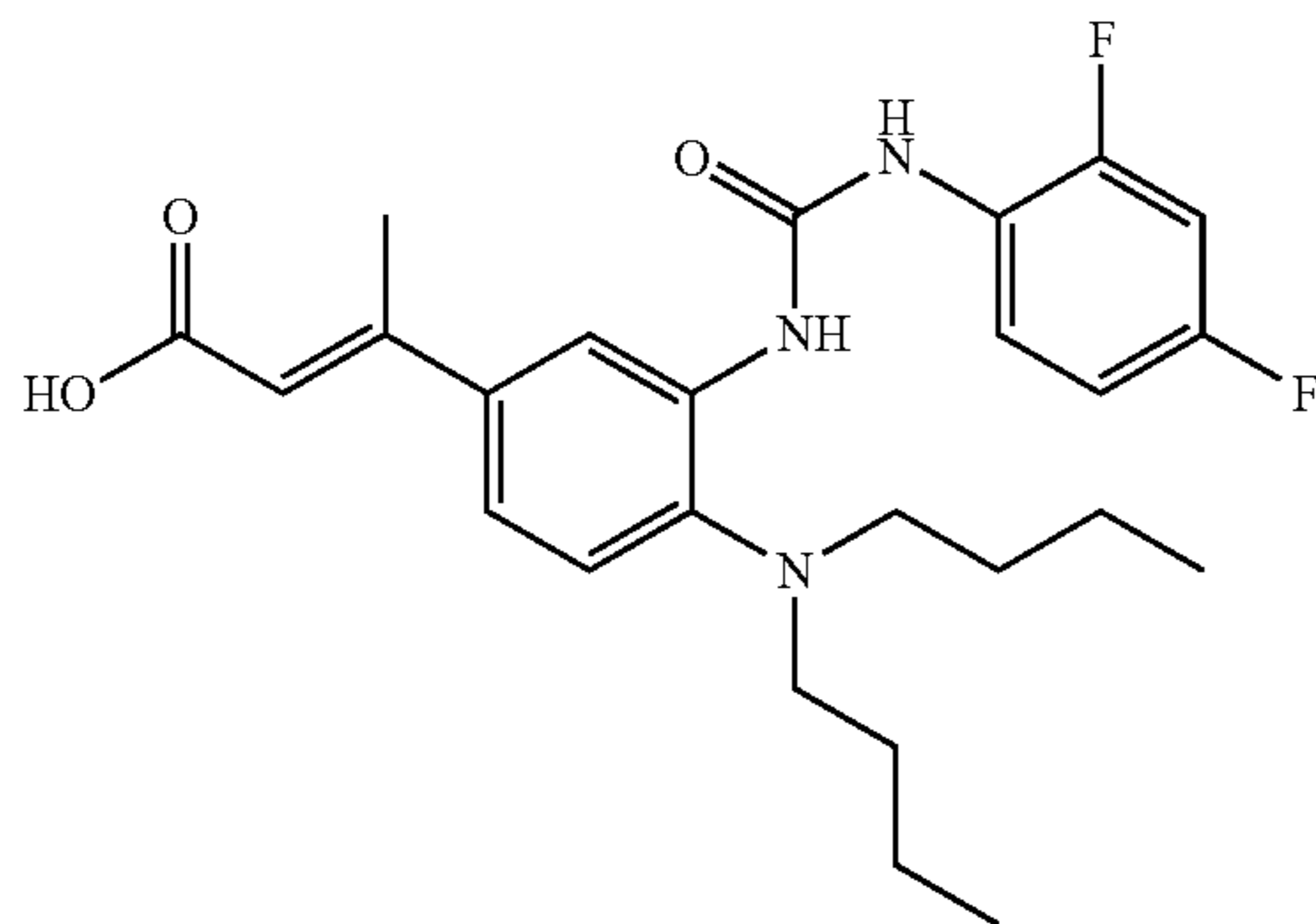


¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.84 (t, J=6.9 Hz, 6H), 1.20-1.30 (m, 11H), 2.30 (s, 3H), 2.52 (s, 3H), 2.86-2.88 (m, 4H), 4.12 (q, J=6.9 Hz, 2H), 6.07 (s, 1H),

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6.87-6.96 (m, 3H), 7.09 (s, 1H), 7.95-8.01 (m, 1H), 8.35 (s, 1H), 8.61 (s, 1H), 9.21 (s, 1H). MS (ESI), m/z (%): 484.36[M+H]⁺. White solid.

Compound 403

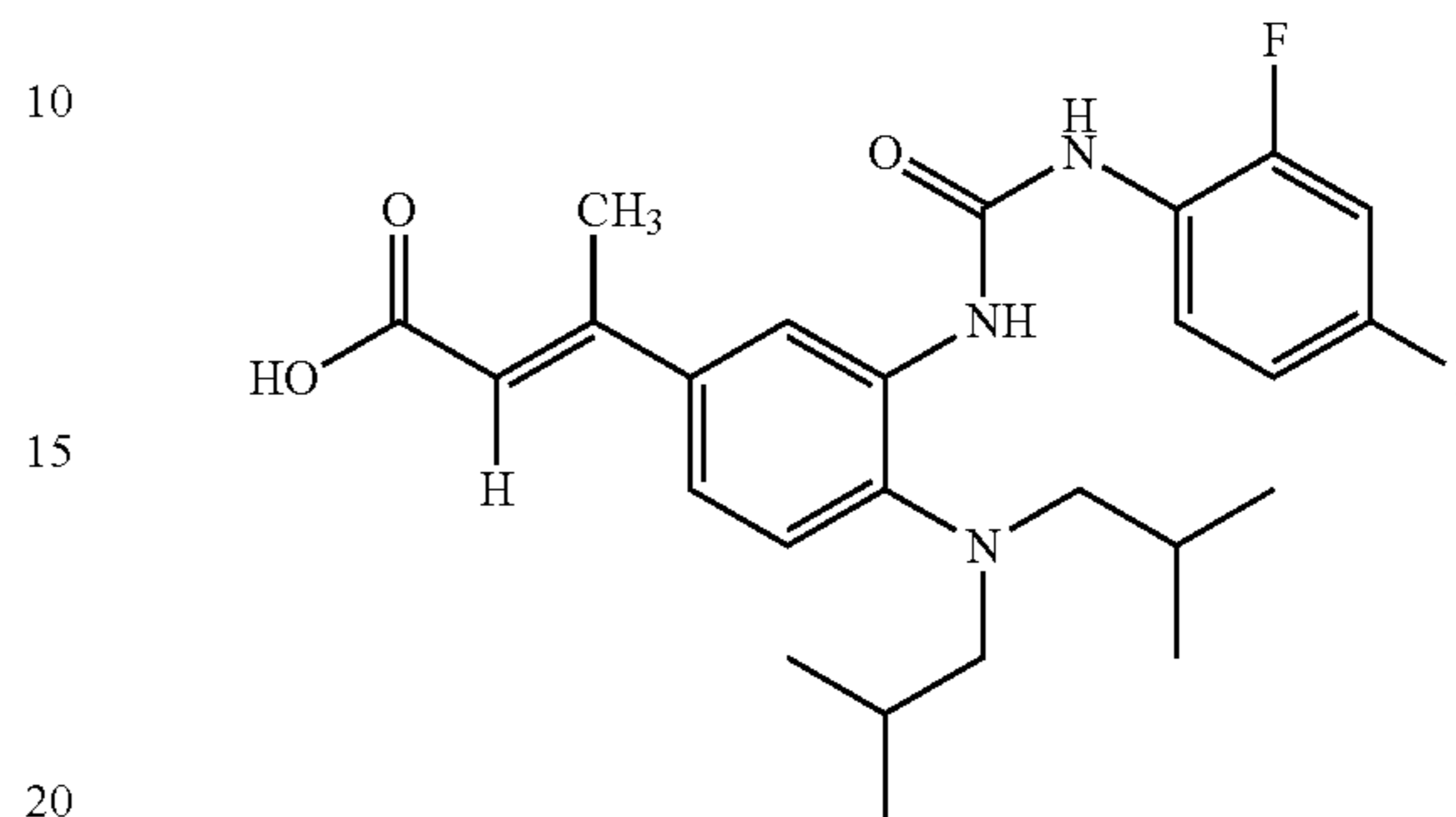


¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.19-1.34 (m, 8H), 2.49 (s, 3H), 2.86-2.91 (m, 4H), 6.05 (s, 1H), 6.91 (t, J=8.7 Hz, 3H), 7.00-7.12 (m, 3H), 8.10-8.19 (m, 1H), 8.32 (s, 1H), 8.26 (s, 1H), 8.63 (s, 1H), 9.32 (s, 1H). MS (ESI), m/z (%): 460.29[M+H]⁺. White solid.

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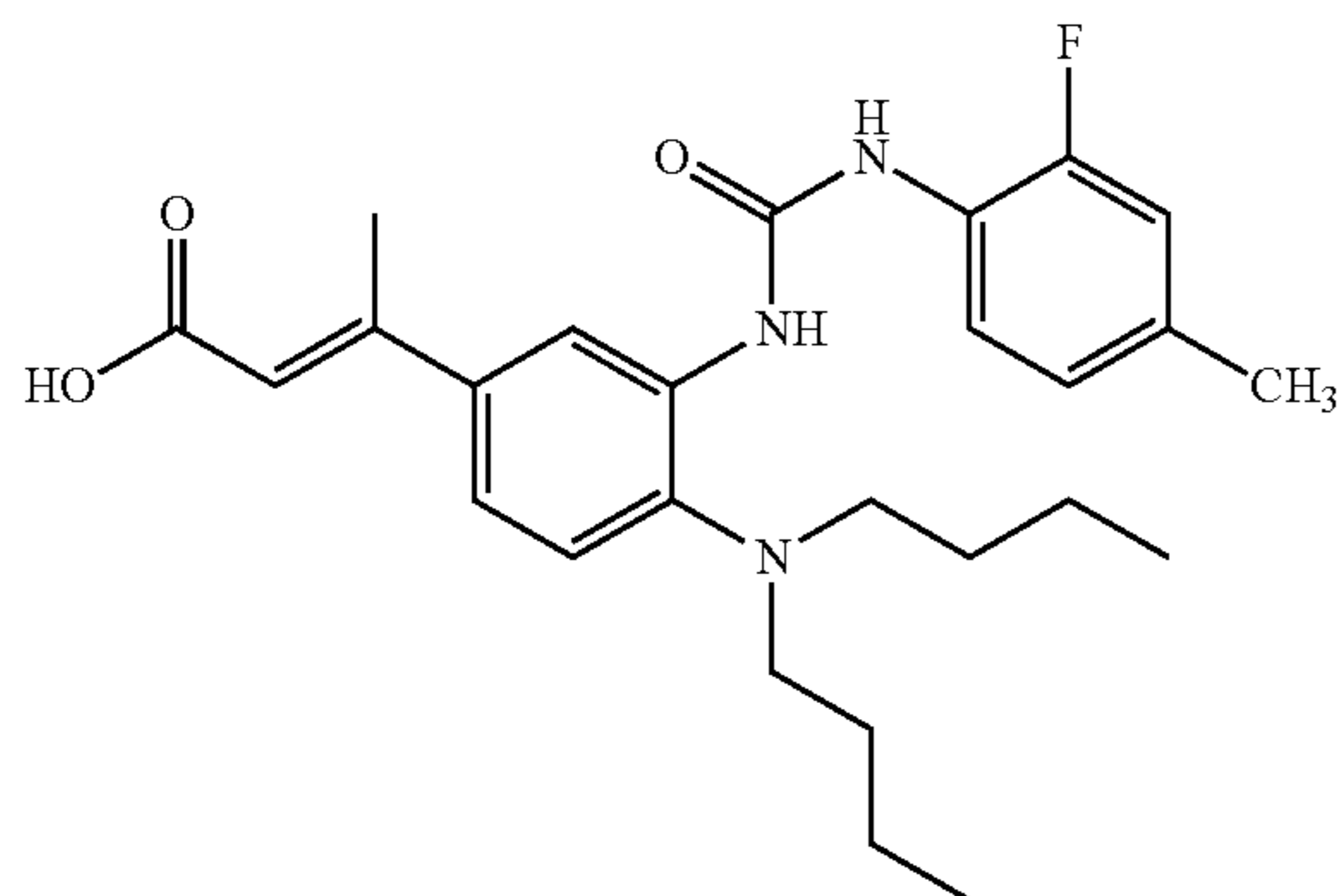
3H), 2.79 (d, J=12.0 Hz, 4H), 4.13 (q, J=6.0 Hz, 2H), 6.09 (s, 1H), 7.03-7.05 (m, 1H), 7.19-7.23 (m, 2H), 7.29-7.31 (t, J=6 Hz, 1H), 7.98-8.01 (m, 1H), 8.05 (d, J=6.0 Hz, 1H), 8.09 (s, 1H), 9.33 (s, 1H). MS (ESI), m/z (%): 488.32[M+H]⁺. White solid.

Compound 571



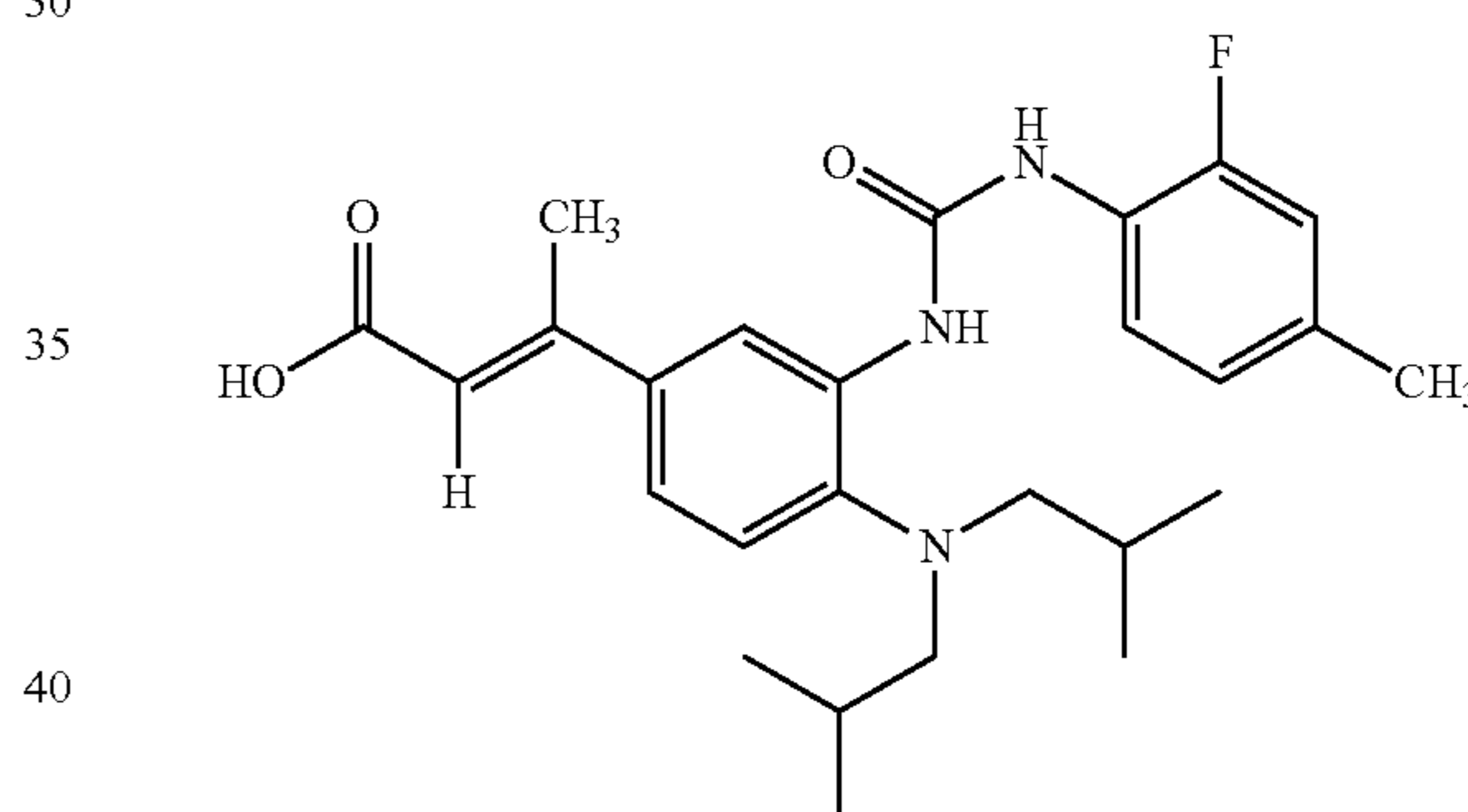
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 9.31 (s, 1H), 8.08 (s, 1H), 8.05 (d, J=6.0 Hz, 1H), 7.98-8.03 (m, 1H), 7.29-7.31 (t, J=6 Hz, 1H), 7.19-7.24 (m, 2H), 7.01-7.06 (m, 1H), 6.05 (s, 1H), 2.86-2.90 (m, 4H), 2.48 (s, 3H), 1.69-1.72 (m, 2H), 0.82 (d, J=6.0 Hz, 12H). MS (ESI), m/z (%): 460.27[M+H]⁺. White solid.

Compound 404



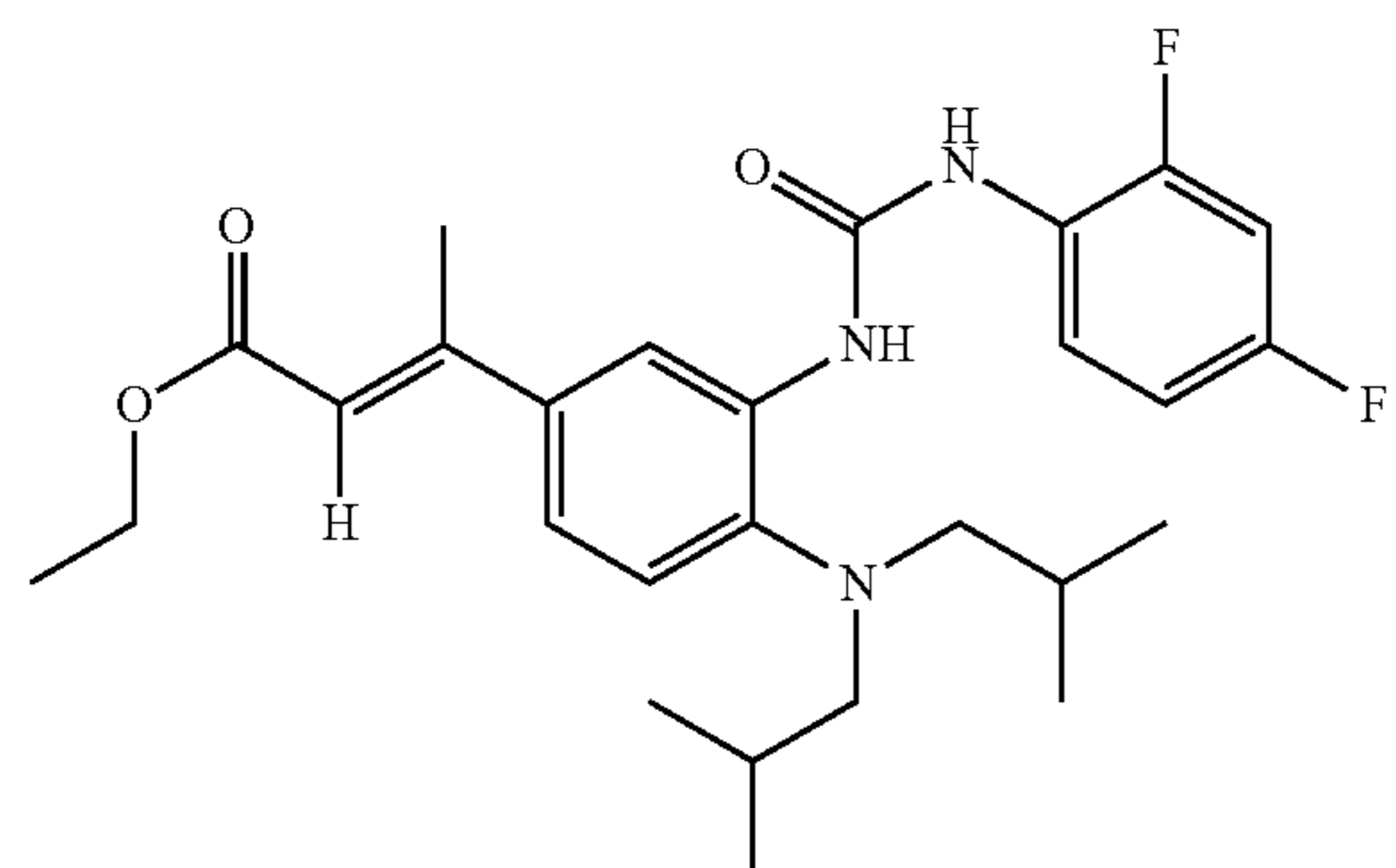
¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.20-1.30 (m, 8H), 1.80 (s, 3H), 2.43 (s, 3H), 2.84-2.89 (m, 4H), 6.05 (s, 1H), 6.86-6.94 (m, 2H), 7.03-7.11 (m, 2H), 7.95-8.00 (m, 1H), 8.29 (s, 1H), 8.59 (s, 1H), 9.19 (s, 1H). MS (ESI), m/z (%): 456.32 [M+H]⁺. White solid.

Compound 572



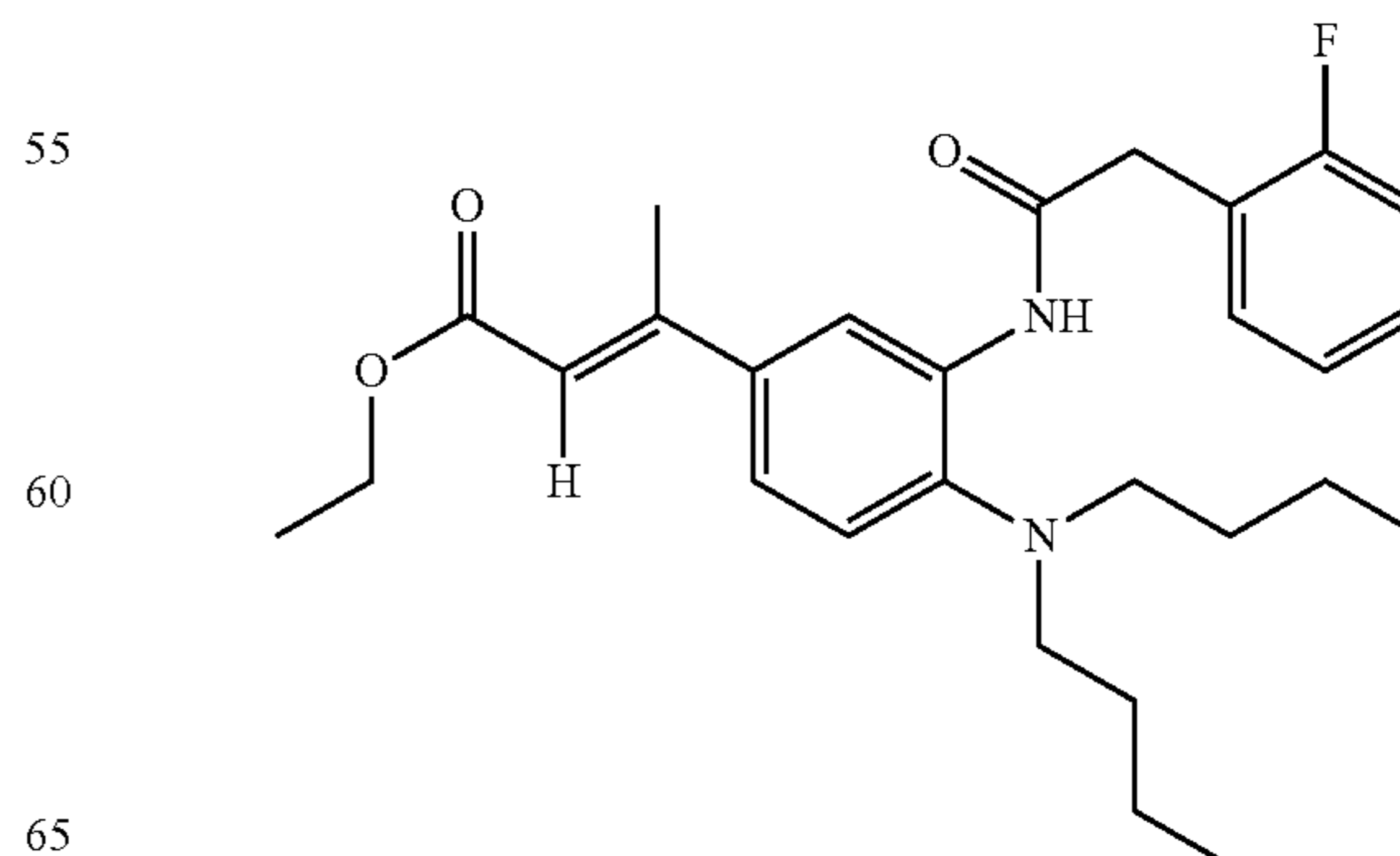
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 12.11 (s, 1H), 9.23 (s, 1H), 8.07 (s, 1H), 8.02 (s, 1H), 7.86 (t, J=8.5 Hz, 1H), 7.19 (s, 2H), 7.06 (d, J=12.2 Hz, 1H), 6.95 (d, J=8.2 Hz, 1H), 6.06 (d, J=1.1 Hz, 1H), 2.77 (d, J=6.9 Hz, 4H), 2.46 (d, J=0.7 Hz, 3H), 2.27 (s, 3H), 1.70 (dt, J=13.4, 6.7 Hz, 2H), 0.83 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 456.30[M+H]⁺. White solid.

Compound 564



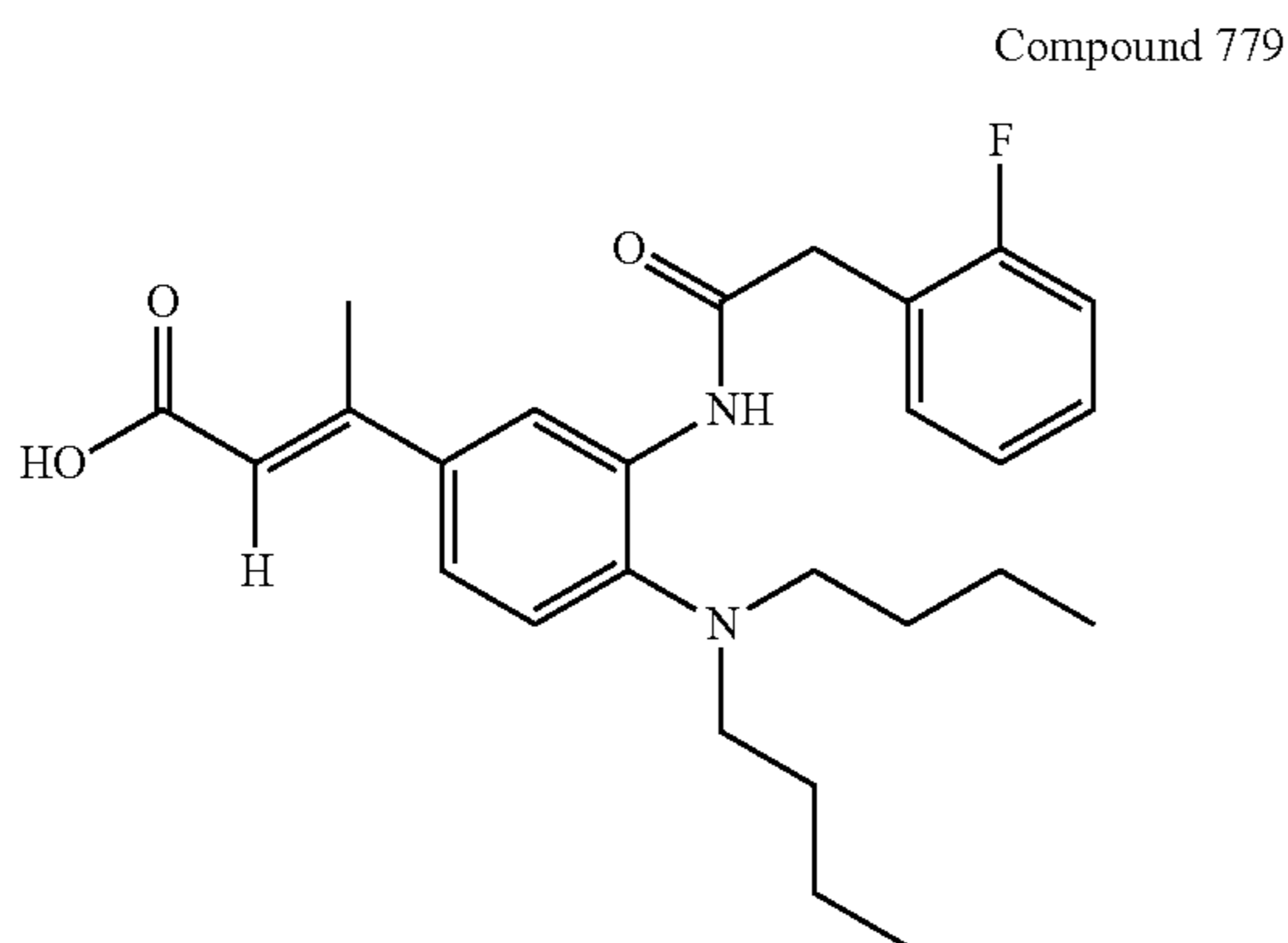
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.83 (d, J=6.0 Hz, 12H), 1.24 (t, J=6.0 Hz, 3H), 1.69-1.72 (m, 2H), 2.49 (s,

Compound 772

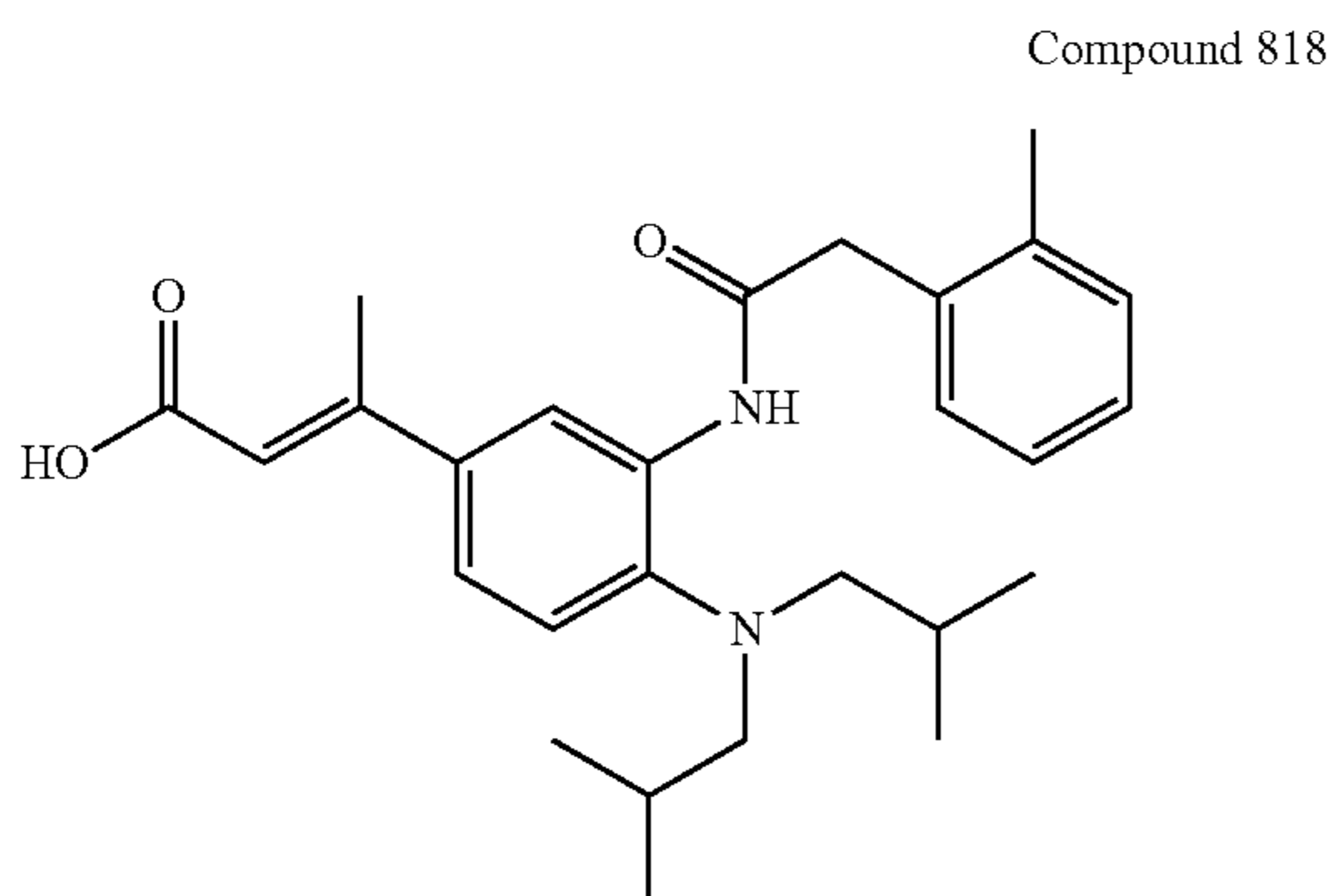


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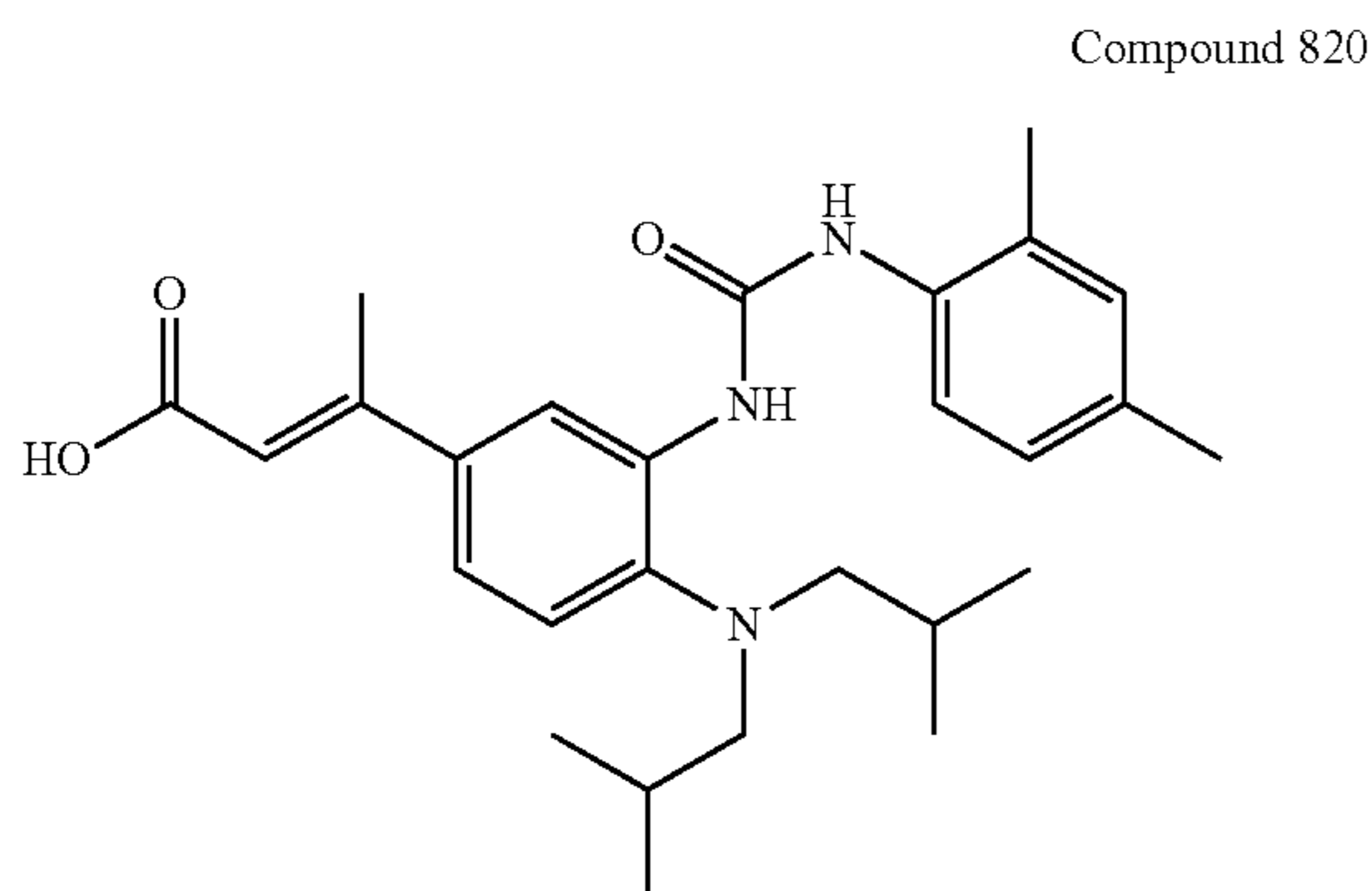
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.80 (t, J=6.0 Hz, 6H), 1.14-1.25 (m, 11H), 2.48 (s, 3H), 2.73 (t, J=6.0 Hz, 4H), 3.83 (s, 2H), 4.13 (q, J=6.0 Hz, 2H), 6.08 (s, 1H), 7.22-7.25 (m, 4H), 7.37-7.40 (m, 1H), 7.46-7.48 (m, 1H), 8.40 (s, 1H), 8.90 (s, 1H). MS (ESI), m/z (%): 469.34 [M+H]⁺. White solid.



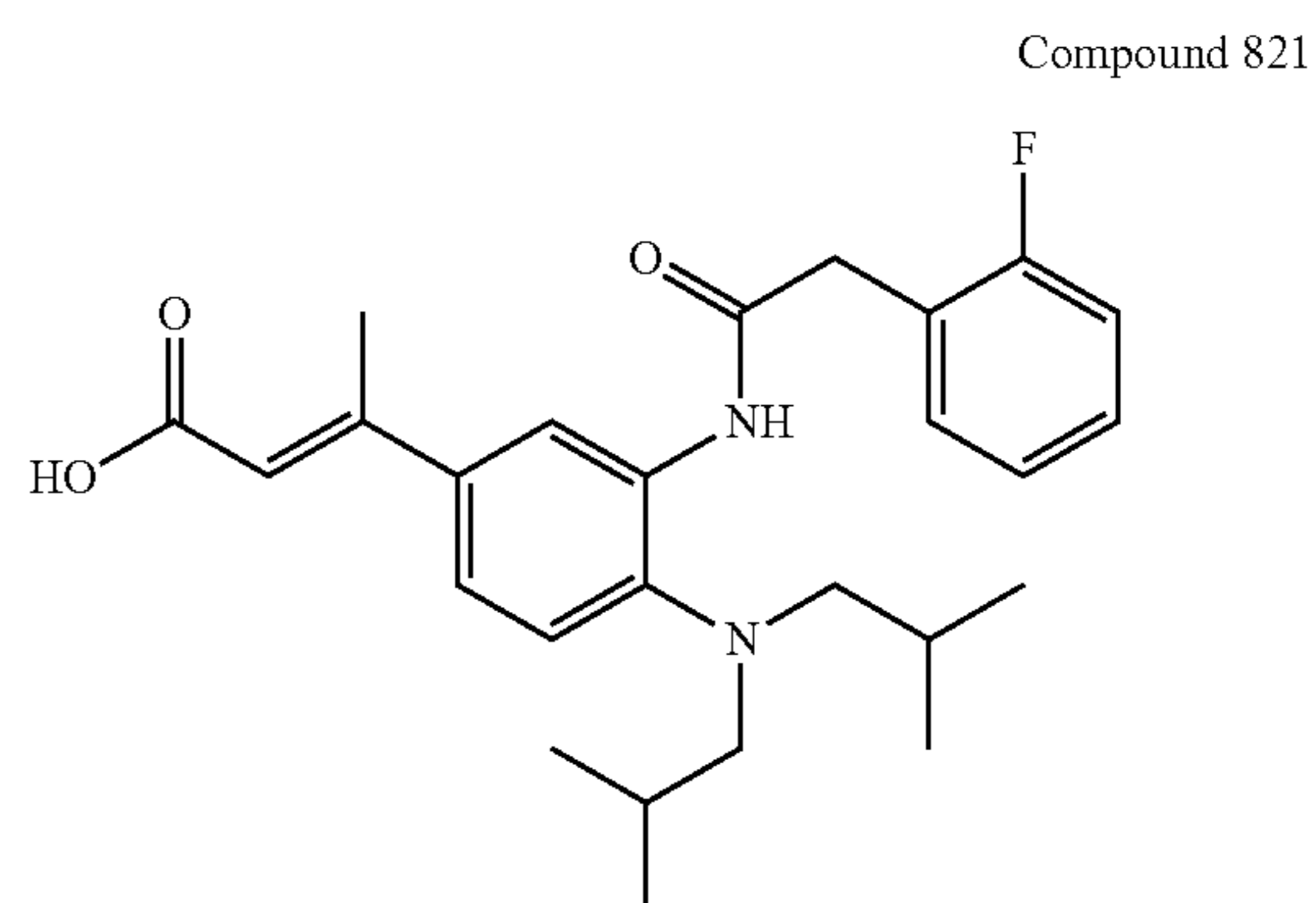
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.80 (t, J=6.0 Hz, 6H), 1.13-1.23 (m, 8H), 2.45 (s, 3H), 2.71 (t, J=6.0 Hz, 4H), 3.83 (s, 2H), 6.05 (s, 1H), 7.22-7.27 (m, 4H), 7.37-7.40 (m, 1H), 7.46-7.48 (m, 1H), 8.39 (s, 1H), 8.89 (s, 1H), 12.18 (s, 1H). MS (ESI), m/z (%): 441.15[M+H]⁺. White solid.



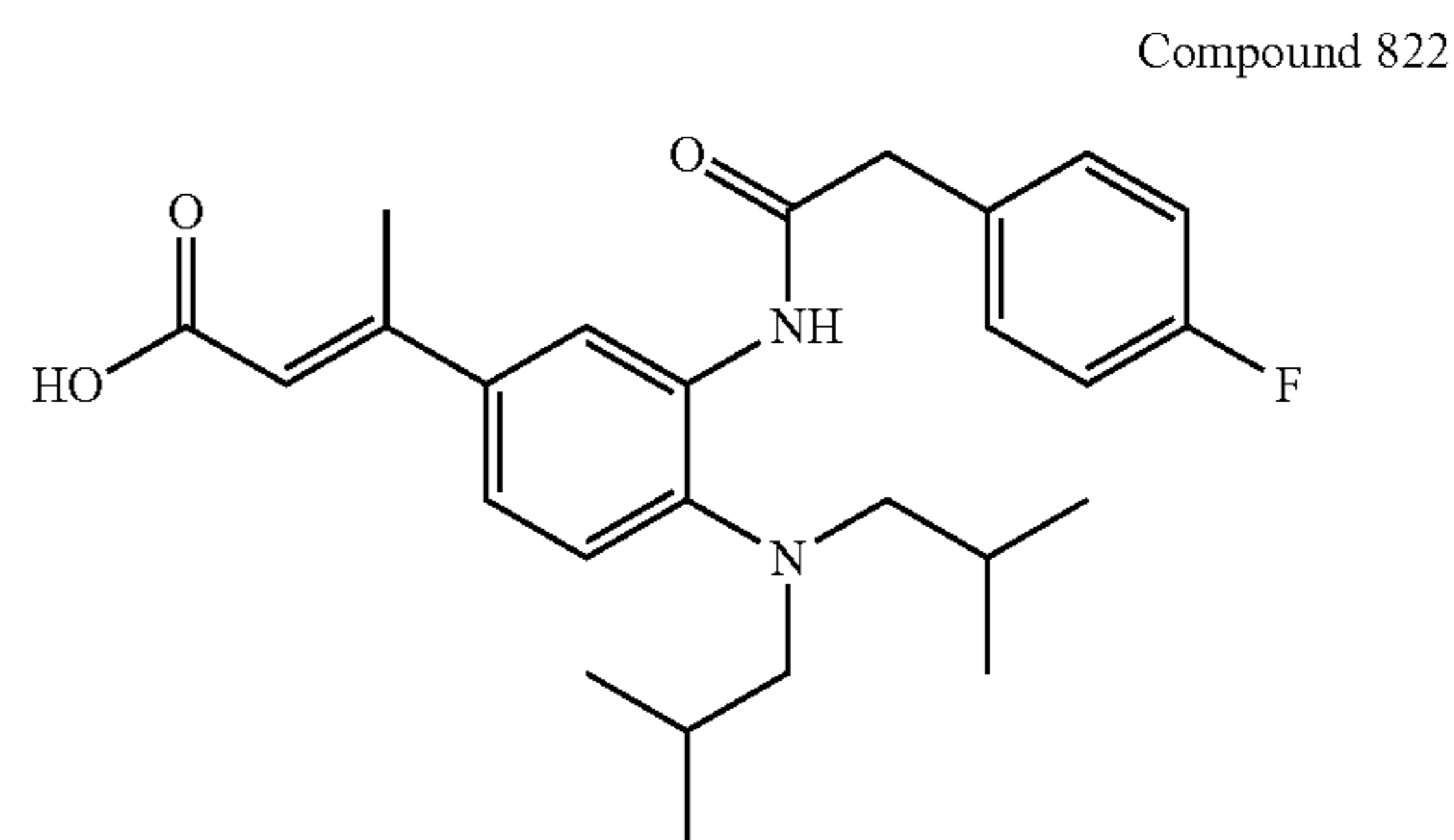
¹H-NMR (400 MHz, DMSO-d₆) δ (ppm): 12.13 (s, 1H), 8.44 (s, 1H), 8.36 (s, 1H), 7.27-7.12 (m, 6H), 6.00 (s, 1H), 3.74 (s, 2H), 2.50 (s, 2H), 2.48 (s, 2H), 2.41 (s, 3H), 2.22 (s, 3H), 1.51 (dt, J=13.1, 6.4 Hz, 2H), 0.69 (d, J=6.5 Hz, 12H). MS (ESI), m/z (%): 437.31 [M+H]⁺. White solid.

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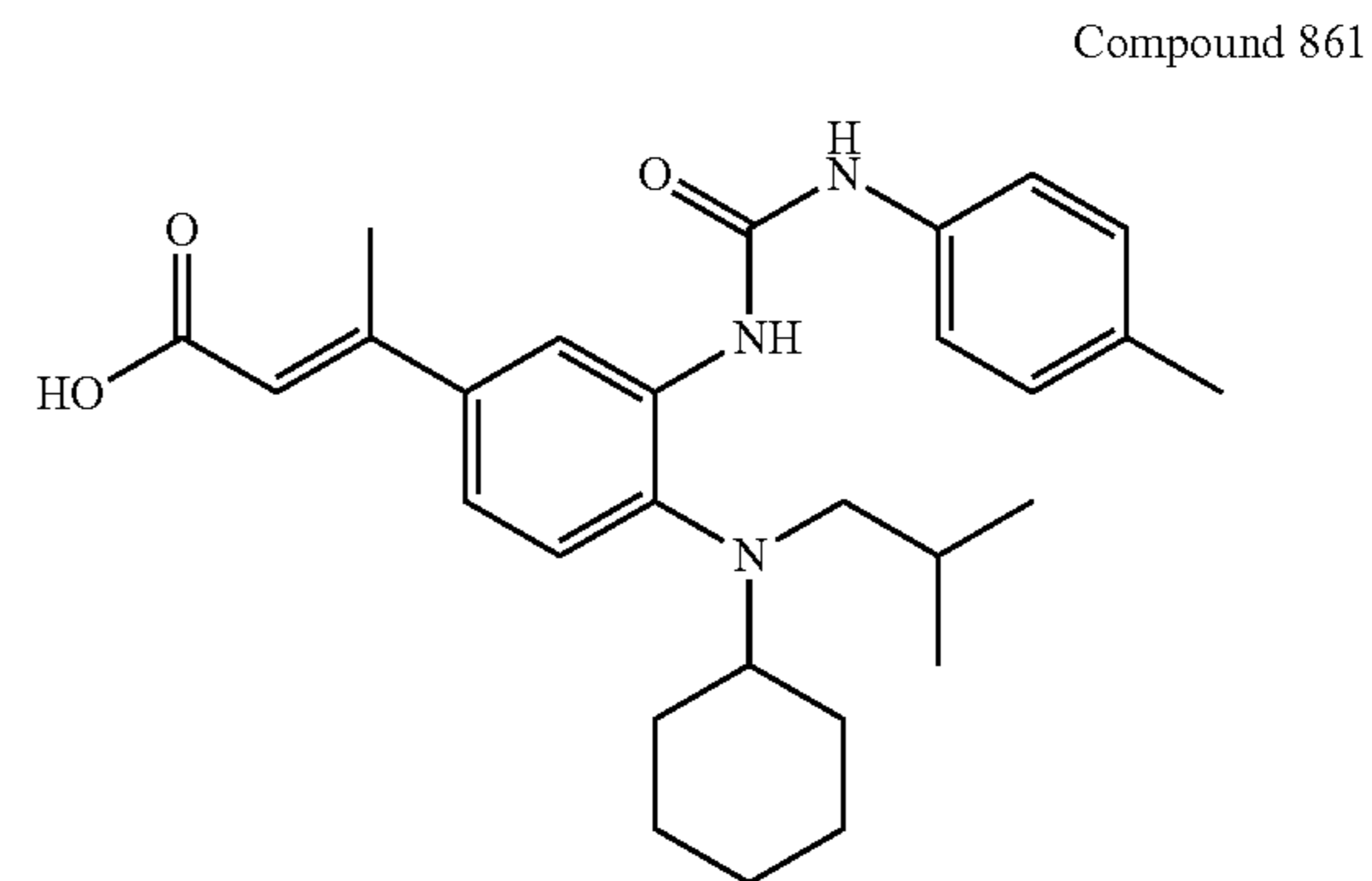
¹H-NMR (400 MHz, DMSO-d₆) δ (ppm): 8.59 (s, 1H), 8.07 (d, J=1.9 Hz, 1H), 7.74 (s, 1H), 7.28 (d, J=8.0 Hz, 1H), 7.13 (dt, J=8.5, 5.3 Hz, 2H), 6.98 (s, 1H), 6.93 (d, J=8.4 Hz, 1H), 6.00 (s, 1H), 2.64 (d, J=6.9 Hz, 4H), 2.42 (s, 3H), 2.21 (s, 3H), 2.15 (s, 3H), 1.60 (dd, J=13.0, 6.4 Hz, 2H), 0.78 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 452.32 [M+H]⁺. White solid.



¹H-NMR (500 MHz, DMSO-d₆) δ (ppm): 12.17 (s, 1H), 8.80 (d, J=15.8 Hz, 1H), 8.33 (s, 1H), 7.43 (t, J=7.4 Hz, 1H), 7.36 (dd, J=13.4, 6.2 Hz, 1H), 7.28 (s, 2H), 7.20 (dd, J=12.6, 5.3 Hz, 2H), 6.05 (s, 1H), 3.85-3.77 (m, 2H), 2.61 (t, J=12.7 Hz, 4H), 2.45 (s, 3H), 1.62 (dt, J=12.0, 6.0 Hz, 2H), 0.79 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 441.27 [M+H]⁺. White solid.

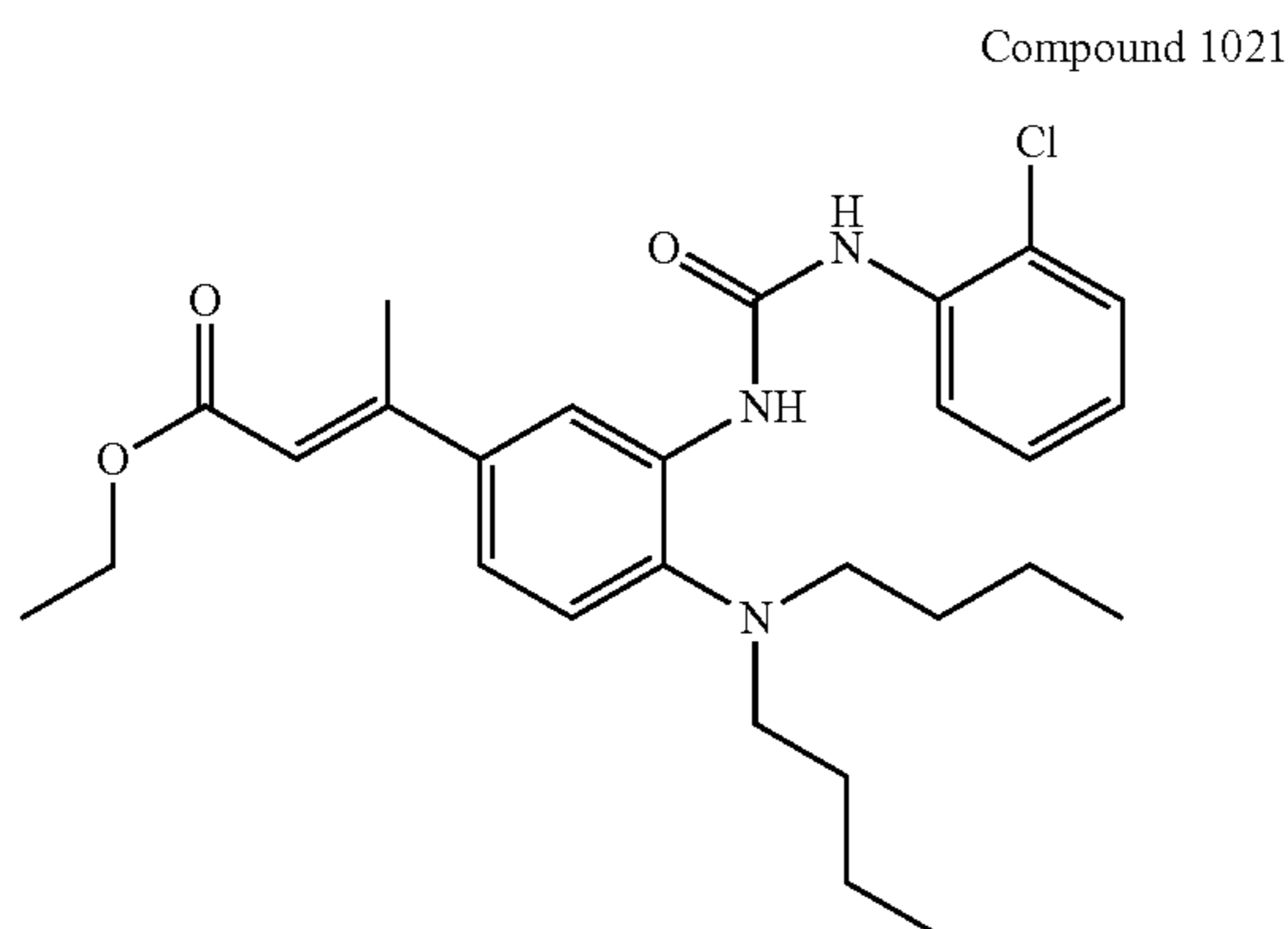


¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 12.16 (s, 1H), 8.72 (d, J=21.6 Hz, 1H), 8.30 (s, 1H), 7.38 (s, 2H), 7.31-7.13 (m, 4H), 6.04 (s, 1H), 3.74 (d, J=18.0 Hz, 2H), 2.59 (t, J=13.6 Hz, 4H), 2.45 (s, 3H), 1.59 (d, J=5.8 Hz, 2H), 0.77 (d, J=5.9 Hz, 12H). MS (ESI), m/z (%): 441.27 [M+H]⁺. White solid.

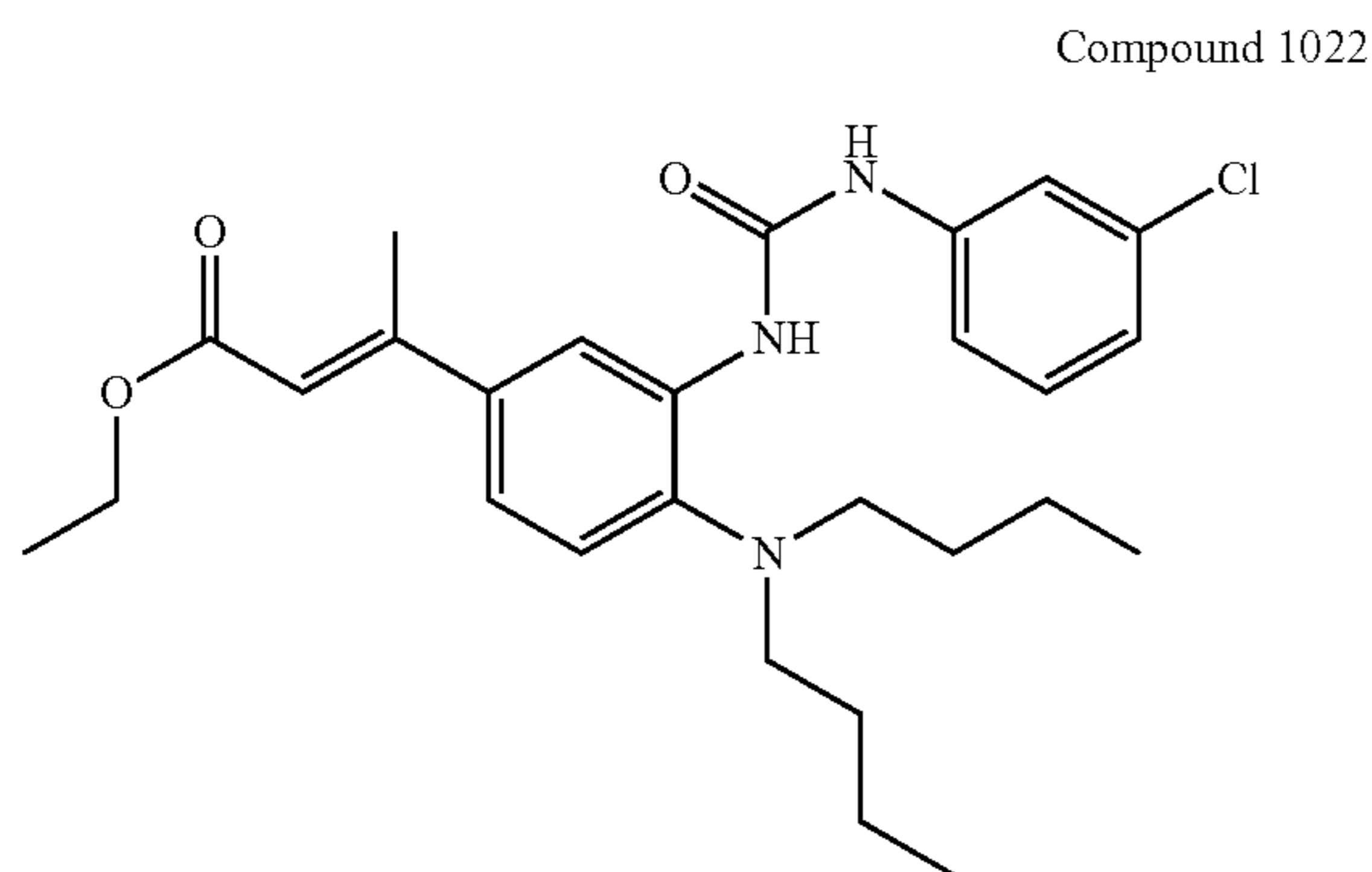


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¹H-NMR (400 MHz, DMSO-d₆) δ 12.12 (s, 1H), 9.42 (s, 1H), 8.20 (d, J=2.1 Hz, 1H), 7.86 (s, 1H), 7.33 (d, J=8.4 Hz, 2H), 7.13 (dt, J=8.4, 5.3 Hz, 2H), 7.06 (d, J=8.3 Hz, 2H), 6.03 (d, J=1.2 Hz, 1H), 2.77 (d, J=5.3 Hz, 2H), 2.53 (t, J=10.7 Hz, 1H), 2.44 (d, J=1.0 Hz, 3H), 2.21 (s, 3H), 1.89-1.79 (m, 2H), 1.64 (d, J=11.7 Hz, 2H), 1.46 (d, J=10.7 Hz, 1H), 1.31 (ddd, J=22.4, 14.4, 7.9 Hz, 2H), 1.14 (ddd, J=30.5, 21.7, 12.0 Hz, 4H), 0.78 (d, J=6.6 Hz, 6H). MS (ESI), m/z (%): 464.33 [M+H]⁺. White solid.



¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.86 (t, J=6.9 Hz, 6H), 1.19-1.37 (m, 11H), 2.53 (s, 3H), 2.89 (t, J=6.6 Hz, 4H), 4.14 (q, J=6.9 Hz, 2H), 6.09 (d, J=1.2 Hz, 1H), 6.90-6.94 (m, 1H), 7.07-7.15 (m, 2H), 7.19-7.28 (m, 2H), 7.72 (d, J=1.8 Hz, 1H), 8.33 (s, 1H), 8.37 (d, J=1.5 Hz, 1H), 9.57 (s, 1H). MS (ESI), m/z (%): 487.30[M+H]⁺. White solid.

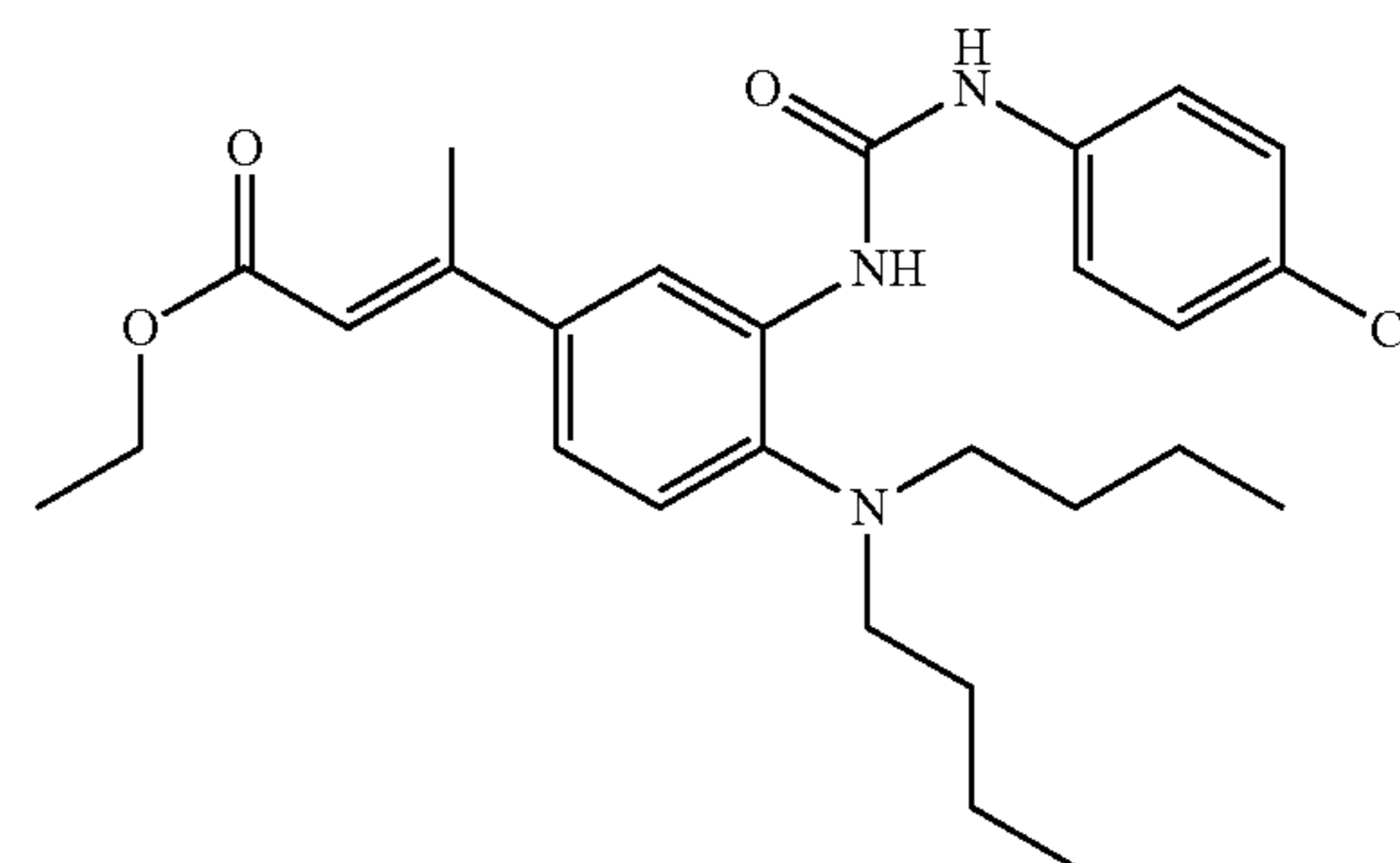


Compound 1022: R² is an ethyl ester group, and the olefinic bond is trans, and the specific structure is as follows:

¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.25-1.35 (m, 11H), 2.50 (s, 3H), 2.89 (m, 4H), 4.09-4.16 (m, 2H), 6.06 (s, 1H), 6.98-7.03 (m, 3H), 7.22-7.27 (m, 1H), 7.35-7.37 (m, 1H), 8.00 (d, J=8.1 Hz, 1H), 8.26 (s, 1H), 8.68 (s, 1H), 8.96 (s, 1H). MS (ESI), m/z (%): 487.29[M+H]⁺. White solid.

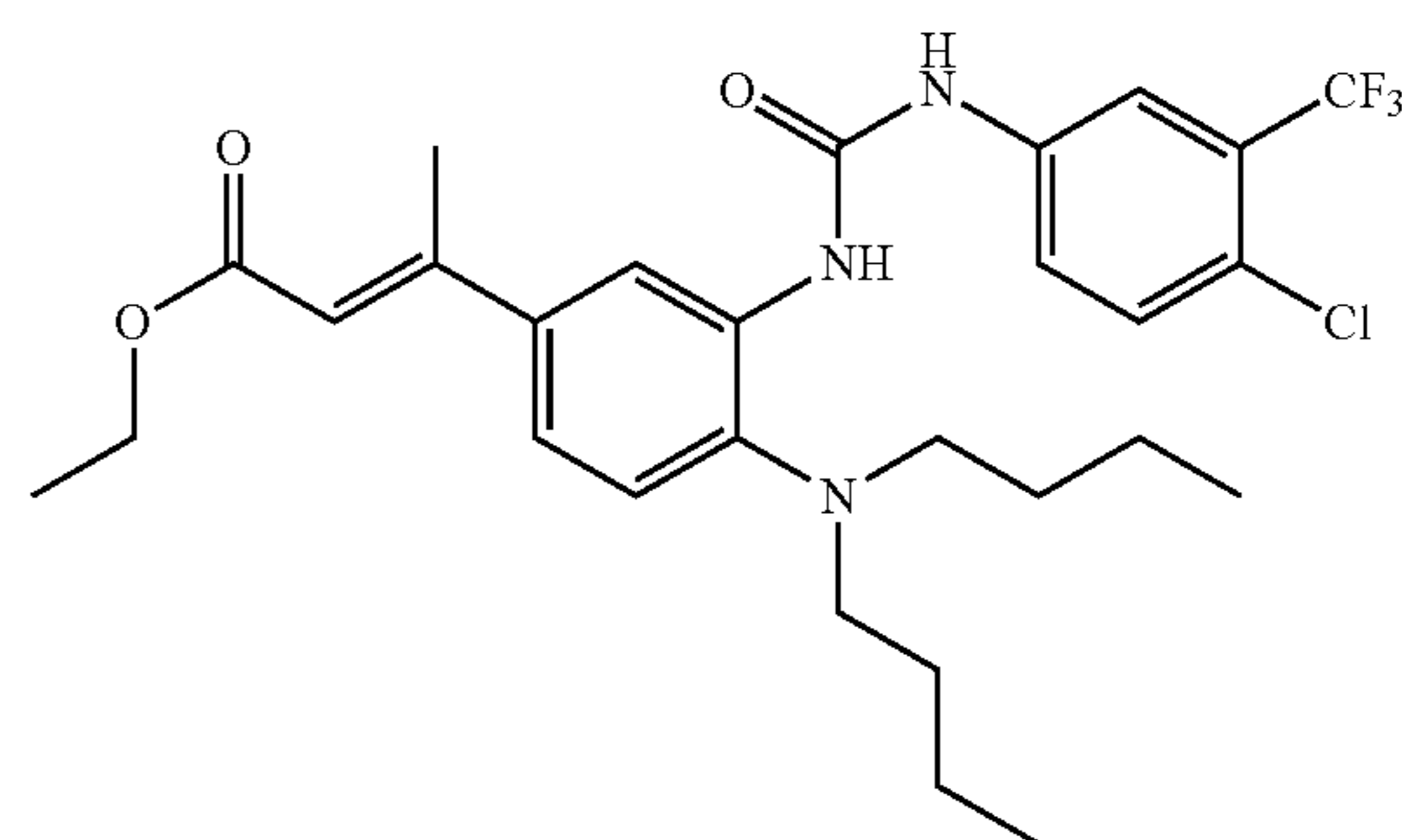
66

Compound 1023



¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.18-1.33 (m, 11H), 2.53 (s, 3H), 2.86-2.92 (m, 4H), 4.13 (q, J=6.9 Hz, 2H), 7.07-7.15 (m, 2H), 7.23 (d, J=-9.0 Hz, 2H), 7.50 (d, J=9.0 Hz, 2H), 8.32 (s, 1H), 8.38 (s, 1H), 9.53 (s, 1H). MS (ESI), m/z (%): 487.29[M+H]⁺. White solid.

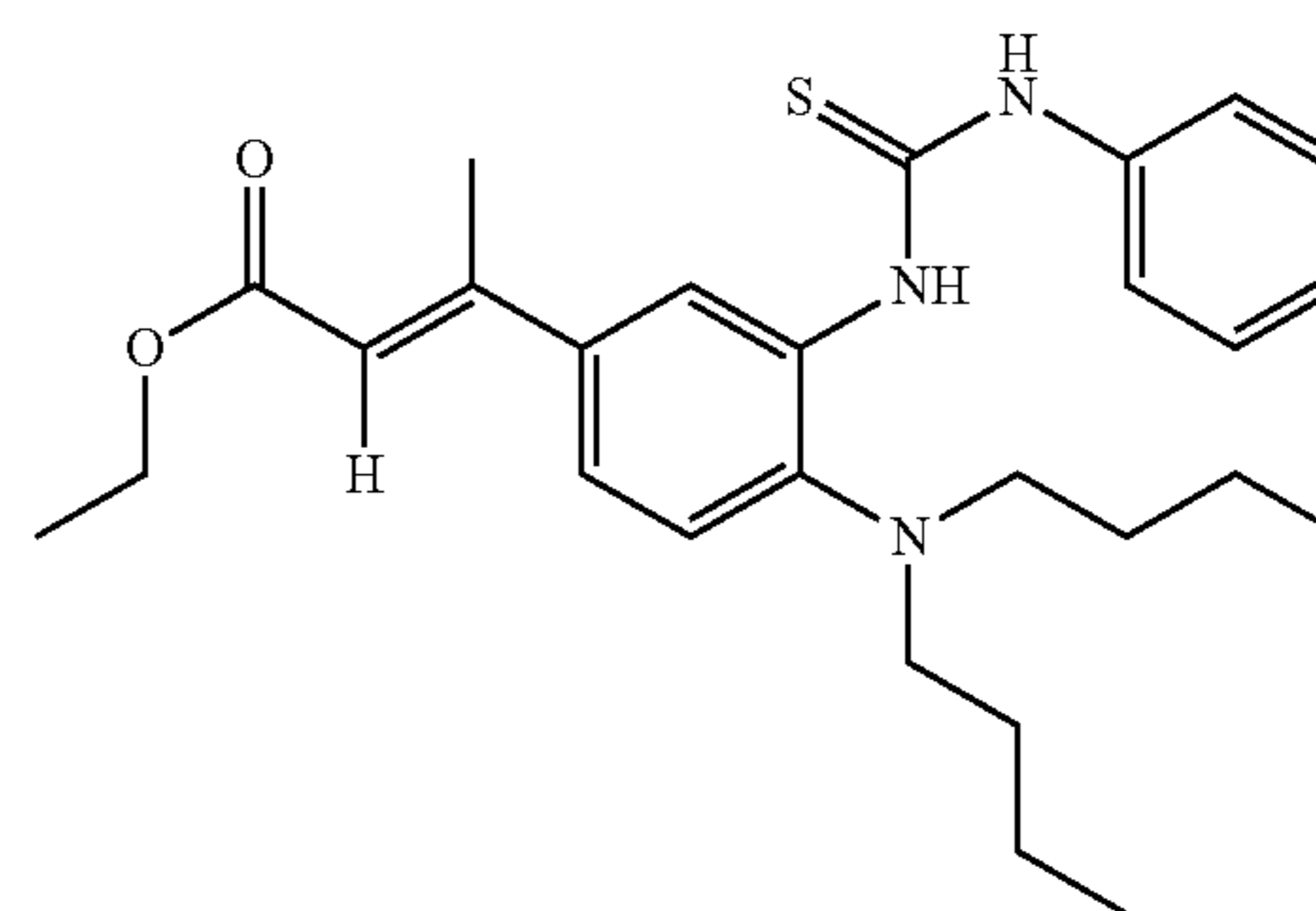
Compound 1024



Compound 1024: R² is an ethyl ester group, and the olefinic bond is trans, and the specific structure is as follows:

¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.18-1.32 (m, 11H), 2.51 (s, 3H), 2.87-2.89 (m, 4H), 4.12 (q, J=6.9 Hz, 2H), 6.07 (s, 1H), 6.91-6.93 (m, 1H), 7.07-7.17 (m, 3H), 8.12-8.14 (m, 1H), 8.33 (s, 1H), 8.36 (s, 1H), 9.31 (s, 1H). MS (ESI), m/z (%): 555.34[M+H]⁺. White solid.

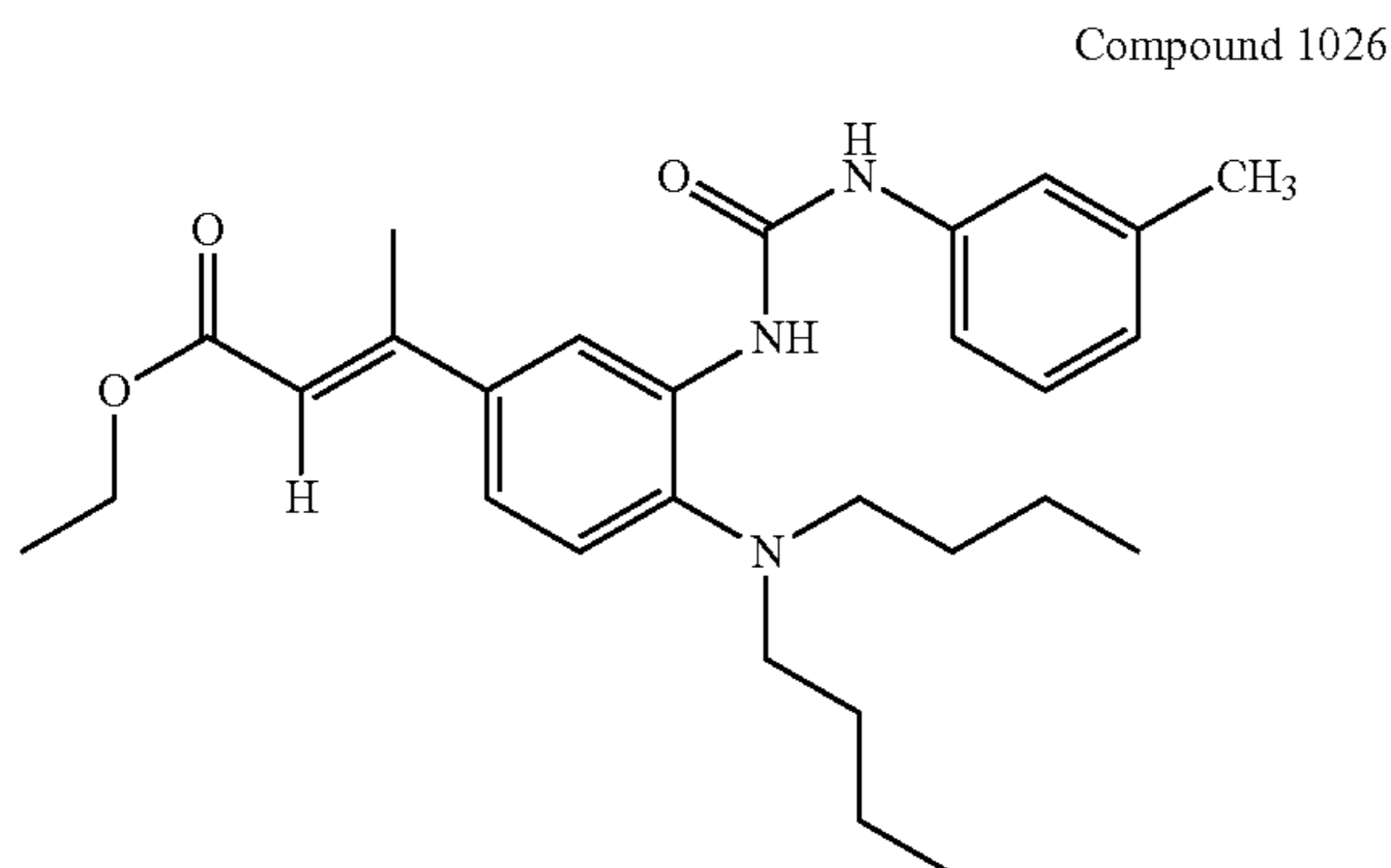
Compound 1025



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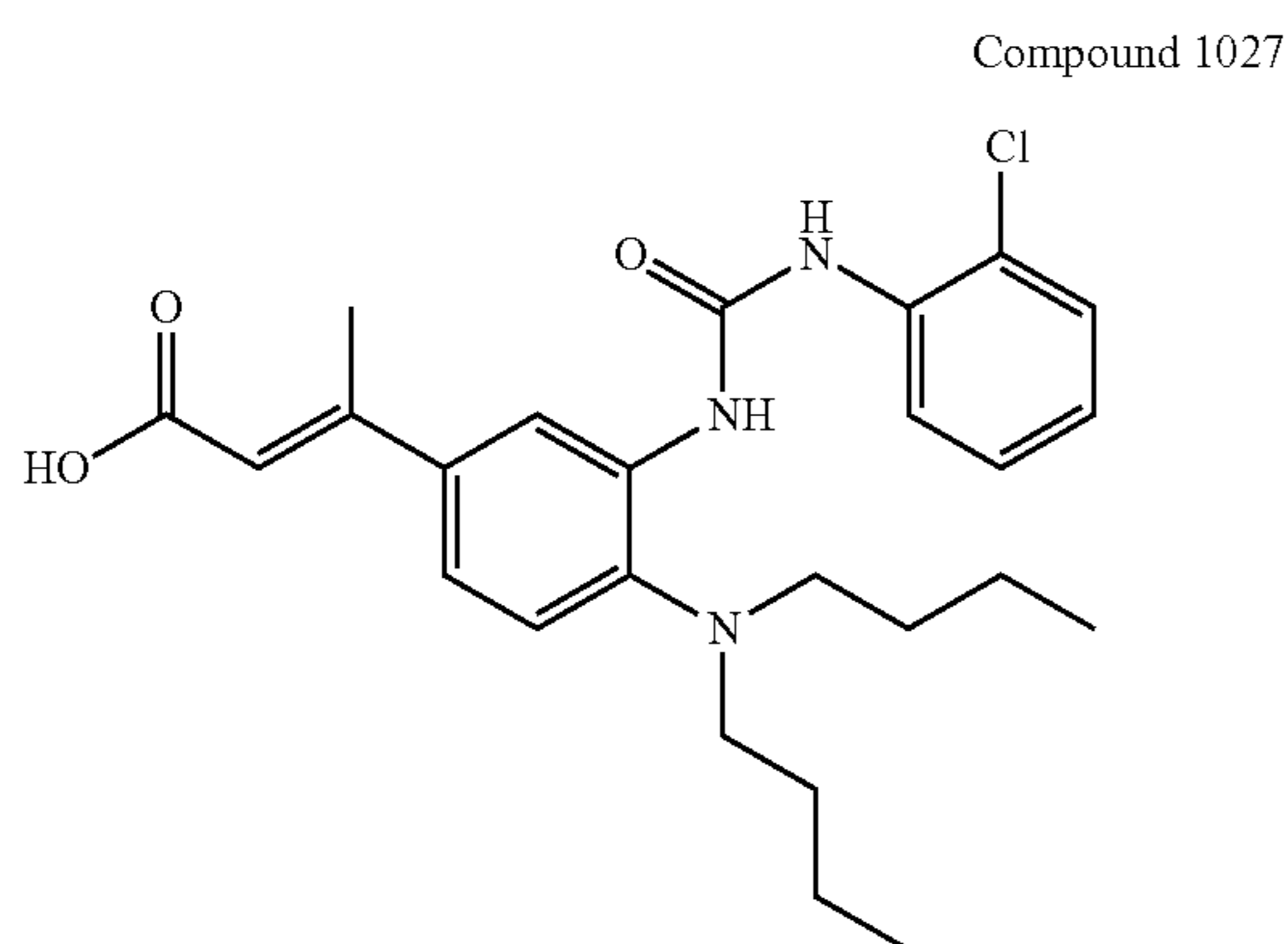
R² is an ethyl ester group, and the olefinic bond is trans, and the specific structure is as follows:

¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.79 (t, J=6.0 Hz, 6H), 1.15 (q, J=6.0 Hz, 4H), 1.23-1.27 (m, 7H), 2.50 (s, 3H), 2.82 (t, J=6.0 Hz, 4H), 3.83 (s, 2H), 4.14 (q, J=6.0, 2H), 6.08 (s, 1H), 7.16 (d, J=12 Hz, 1H), 7.22 (t, J=12 Hz, 1H), 7.34 (d, J=6.0 Hz, 1H), 7.39 (dd, J=12.0, 6.0 Hz, 2H), 7.48 (d, J=6.0 Hz, 2H), 8.45 (s, 1H), 8.97 (s, 1H), 10.37 (s, 1H). MS (ESI), m/z (%): 468.31 [M+H]⁺. White solid.



R² is an ethyl ester group, and the olefinic bond is trans, and the specific structure is as follows:

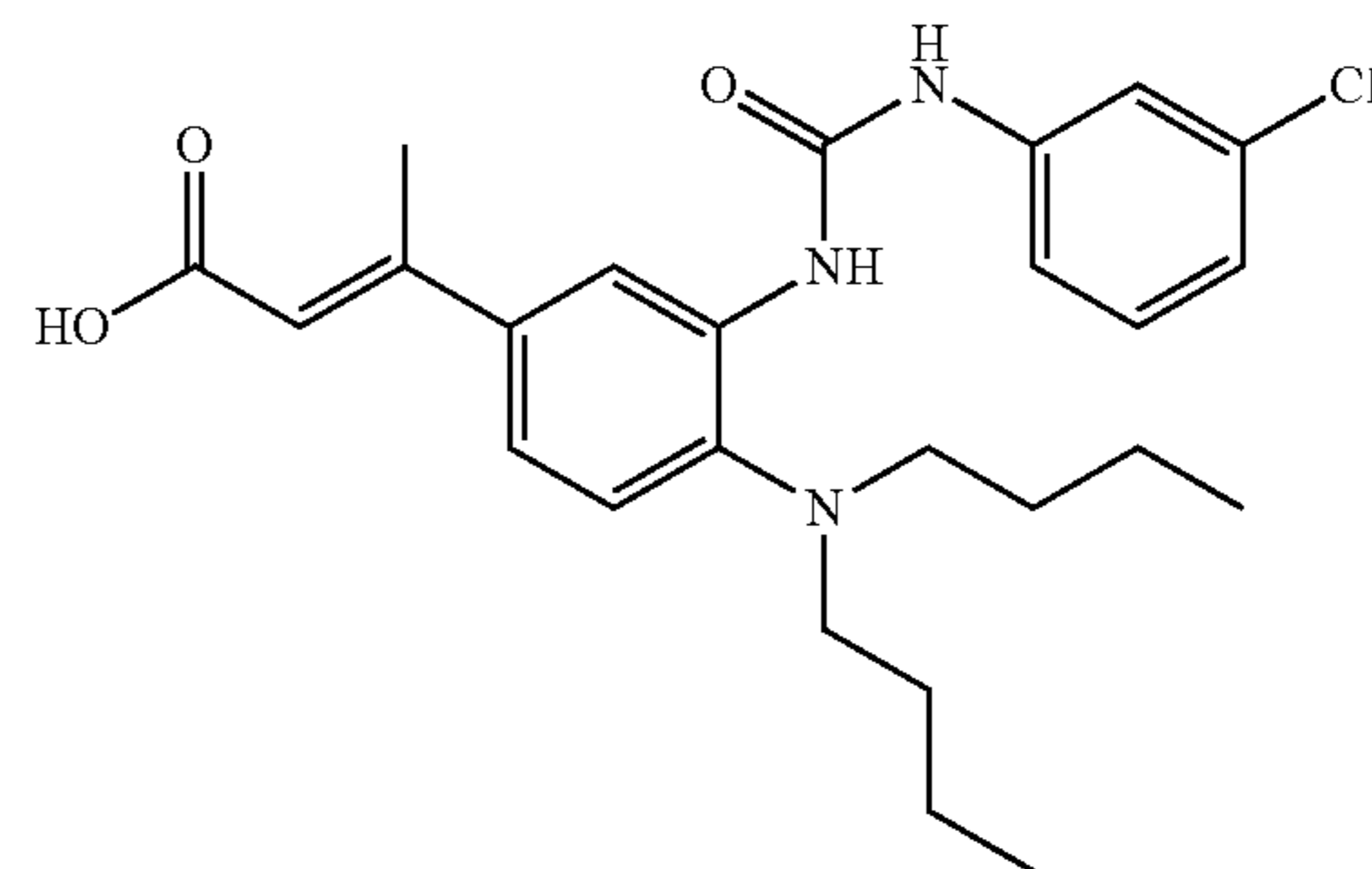
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.81 (t, J=6.0 Hz, 6H), 1.21-1.29 (m, 11H), 2.29 (s, 3H), 2.51 (s, 3H), 2.90 (t, J=6.0 Hz, 4H), 4.15 (q, J=6.0 Hz, 4H), 6.11 (s, 1H), 6.80 (d, J=6.0 Hz, 1H), 7.15-7.25 (m, 4H), 7.36 (s, 1H), 8.35 (s, 1H), 8.39 (d, J=6.0 Hz, 1H), 9.49 (s, 1H). MS (ESI), m/z (%): 466.36[M+H]⁺. White solid.



¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.83 (t, J=6.0 Hz, 6H), 1.13-1.33 (m, 8H), 2.50 (s, 3H), 2.86-2.92 (m, 4H), 6.10 (s, 1H), 7.07-7.09 (m, 1H), 7.13-7.22 (m, 1H), 7.29-7.32 (m, 2H), 7.47 (d, J=12 Hz, 1H), 7.97 (s, 1H), 8.21 (s, 1H), 8.75 (s, 1H), 9.18 (s, 1H). MS (ESI), m/z (%): 459.27 [M+H]⁺. White solid.

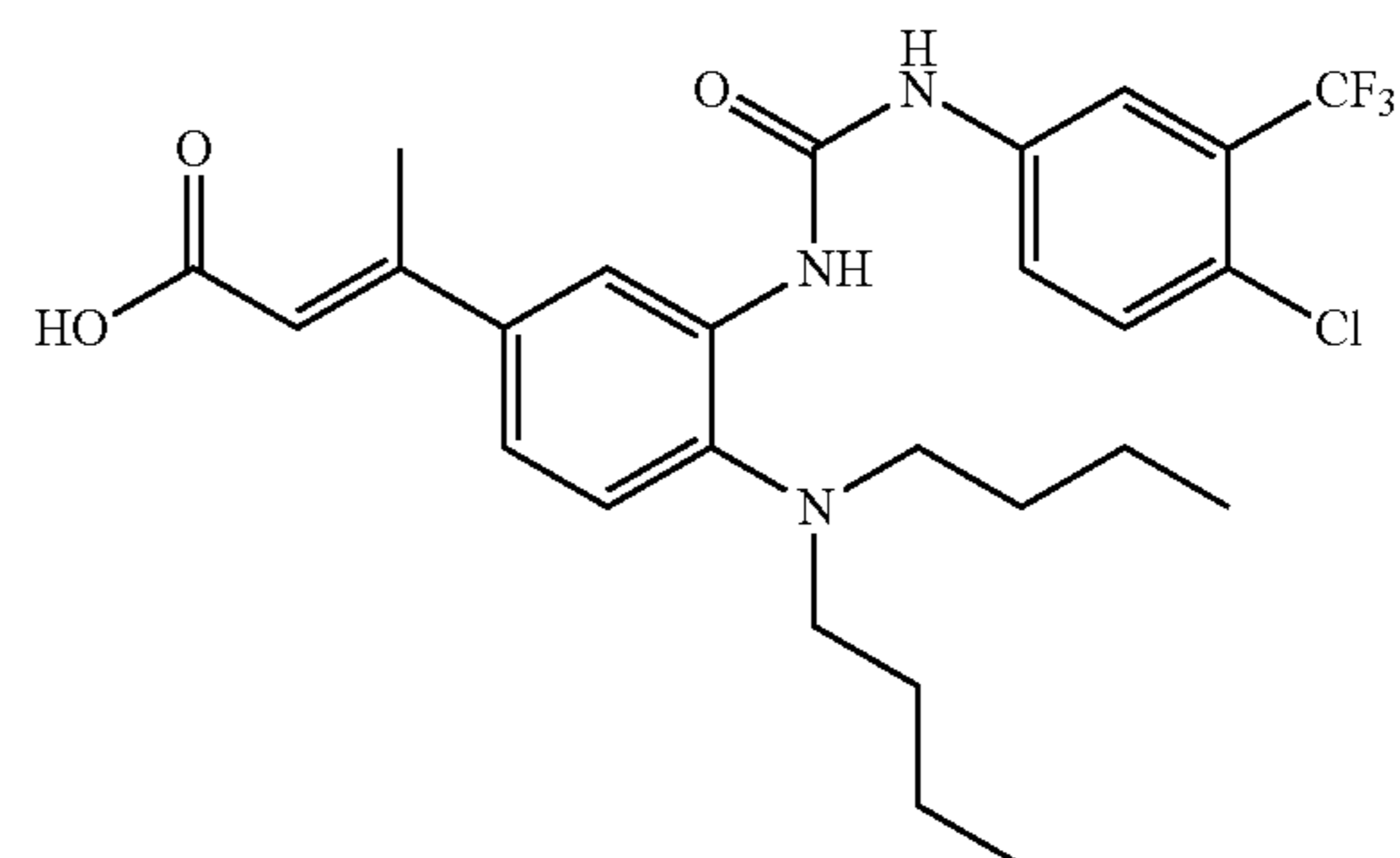
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Compound 1028



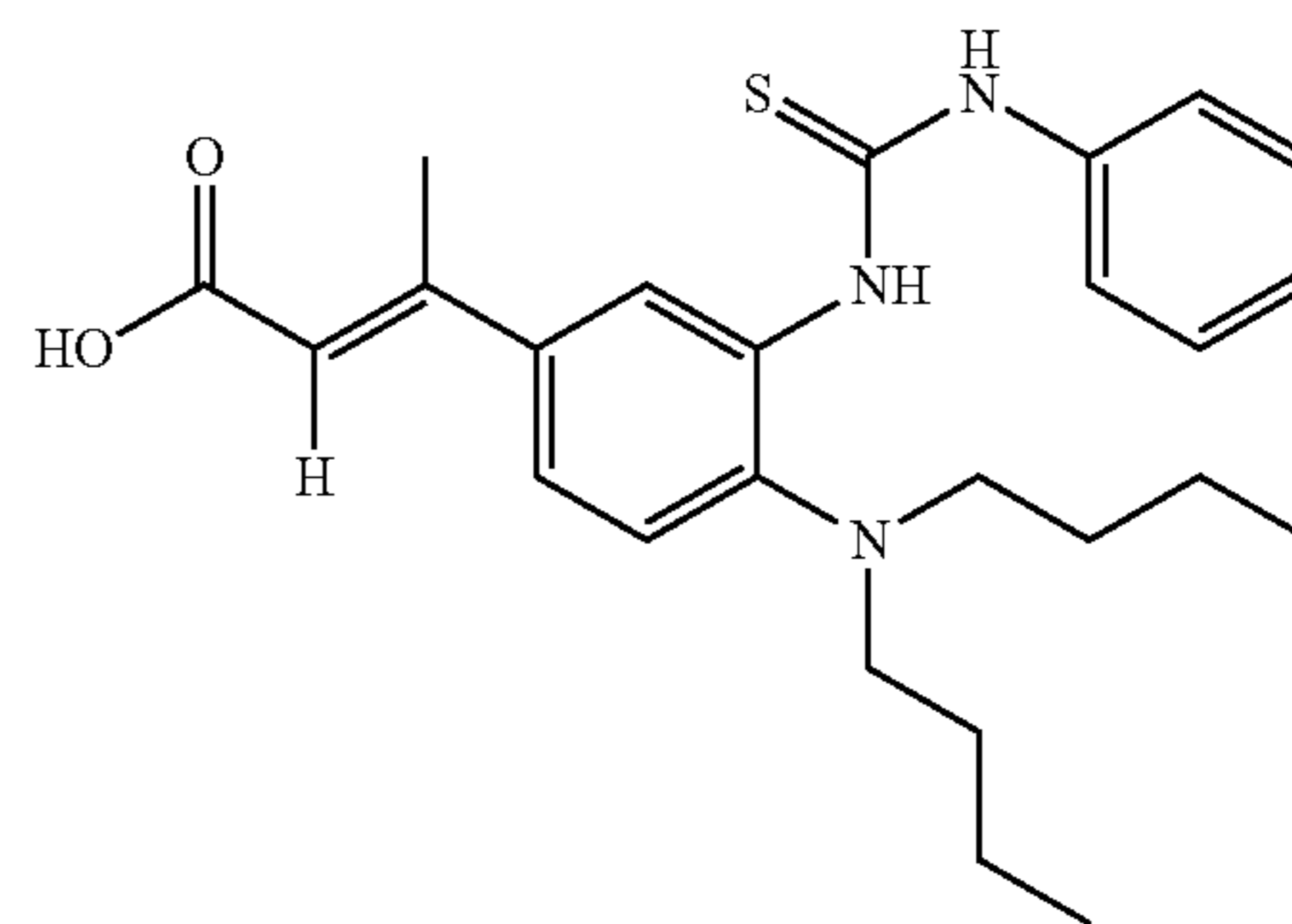
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.0 Hz, 6H), 1.21-1.31 (m, 8H), 2.50 (s, 3H), 2.92 (m, 4H), 4.09-4.16 (m, 2H), 6.10 (s, 1H), 7.02-7.03 (m, 1H), 7.27-7.33 (m, 3H), 7.76 (m, 1H), 8.01 (d, J=7.8 Hz, 1H), 8.32 (s, 1H), 8.47 (s, 1H), 9.84 (s, 1H). MS (ESI), m/z (%): 459.29 [M+H]⁺. White solid.

Compound 1030



¹H-NMR (300 MHz, DMSO-d₆) δ (ppm): 0.85 (t, J=6.9 Hz, 6H), 1.24-1.30 (m, 8H), 2.56 (s, 3H), 2.87-2.90 (m, 4H), 6.05 (s, 1H), 7.12-7.16 (m, 2H), 7.46-7.50 (m, 1H), 7.71 (d, J=8.1 Hz, 1H), 8.35-8.38 (m, 2H), 9.85 (s, 1H). MS (ESI), m/z (%): 527.29[M+H]⁺. White solid.

Compound 1031

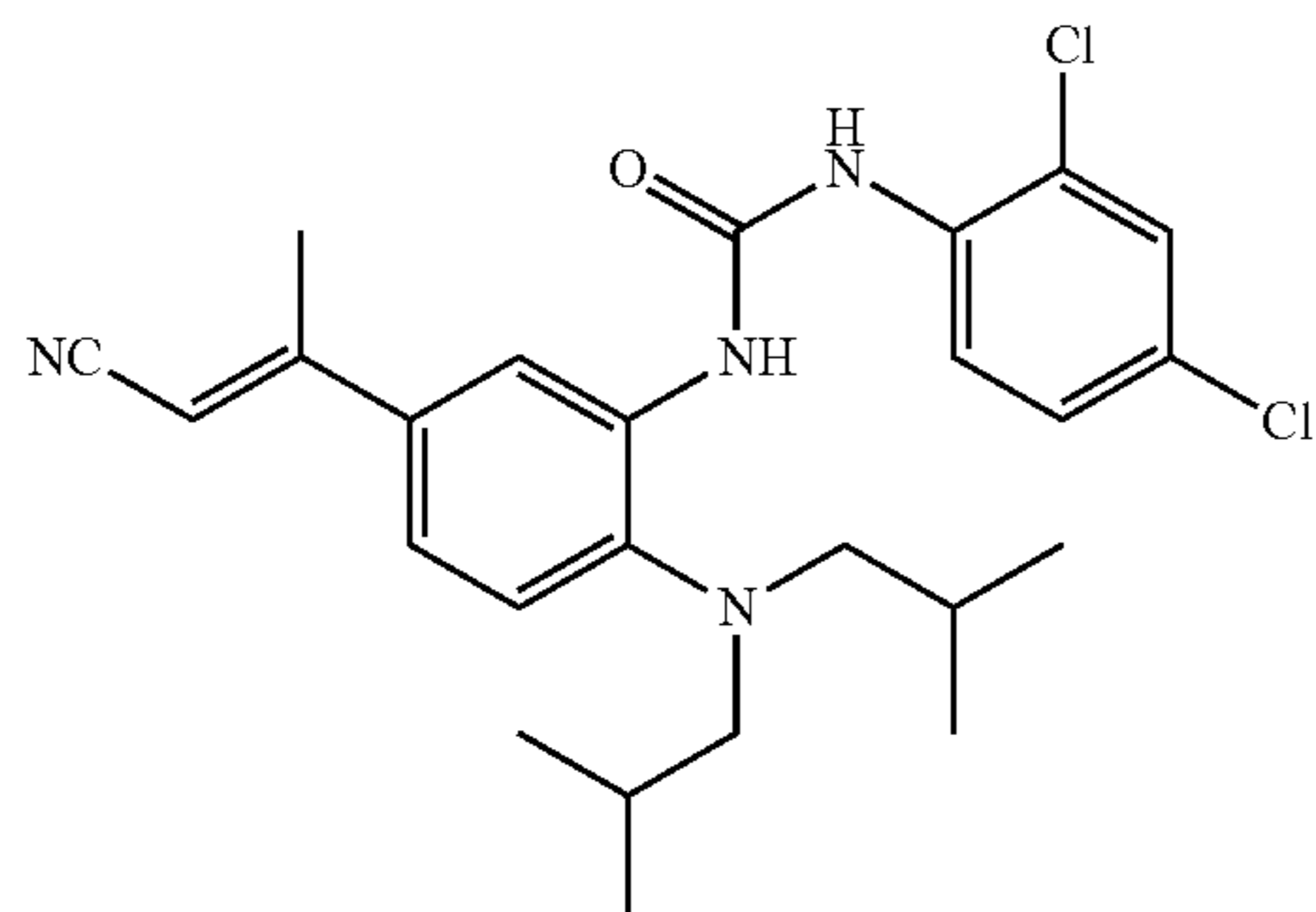


The olefinic bond is trans, Y is S substituted, and R is hydrogen. The specific structure is as follows:

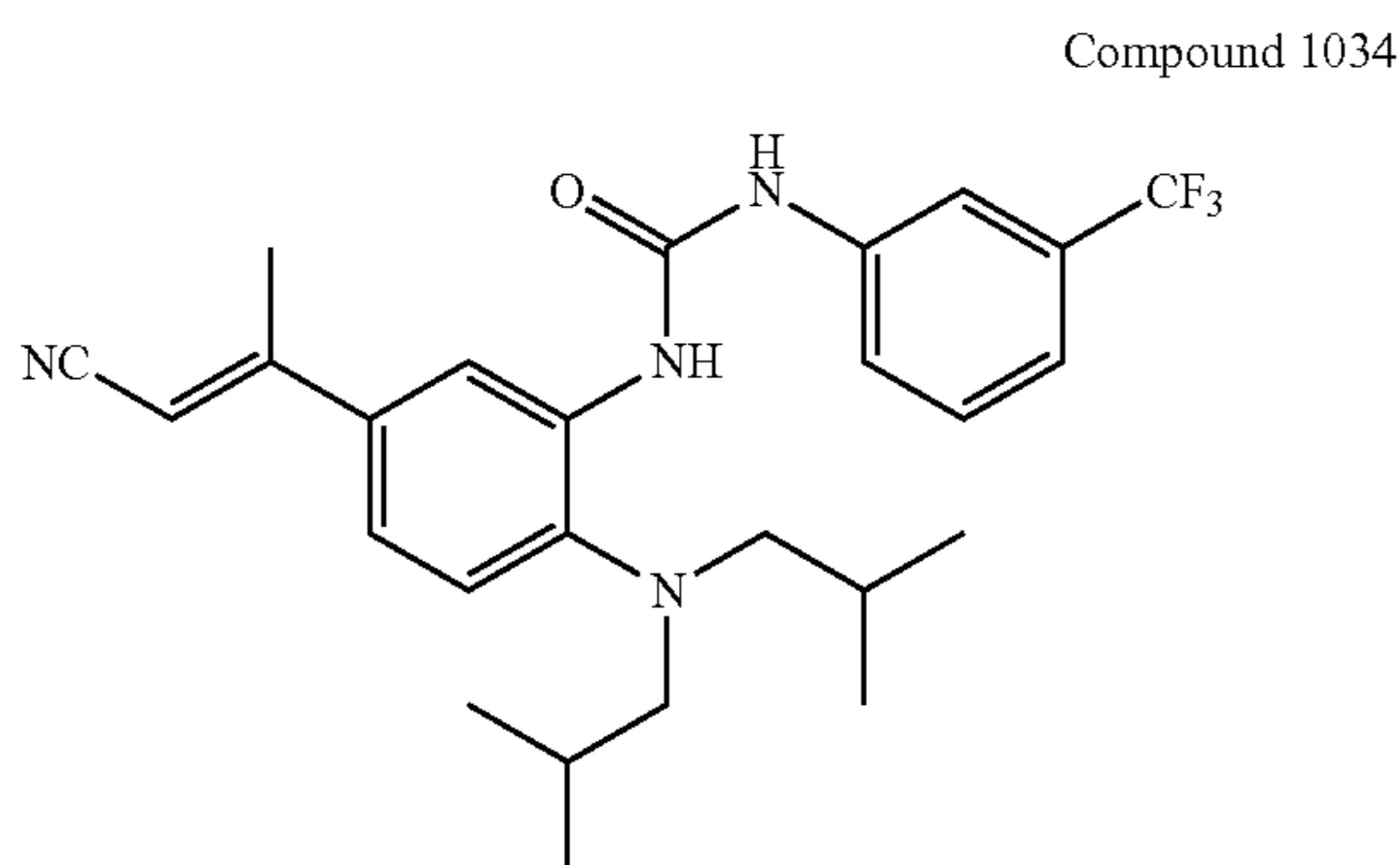
¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 0.80 (t, J=6.0 Hz, 6H), 1.16 (q, J=6.0 Hz, 4H), 1.22-1.28 (m, 4H), 2.51 (s, 3H), 2.80 (t, J=6.0 Hz, 4H), 3.85 (s, 2H), 6.09 (s, 1H), 7.17 (d, J=12 Hz, 1H), 7.23 (t, J=12 Hz, 1H), 7.33 (d, J=6.0 Hz, 1H), 7.39 (dd, J=12.0, 6.0 Hz, 2H), 7.47 (d, J=6.0 Hz,

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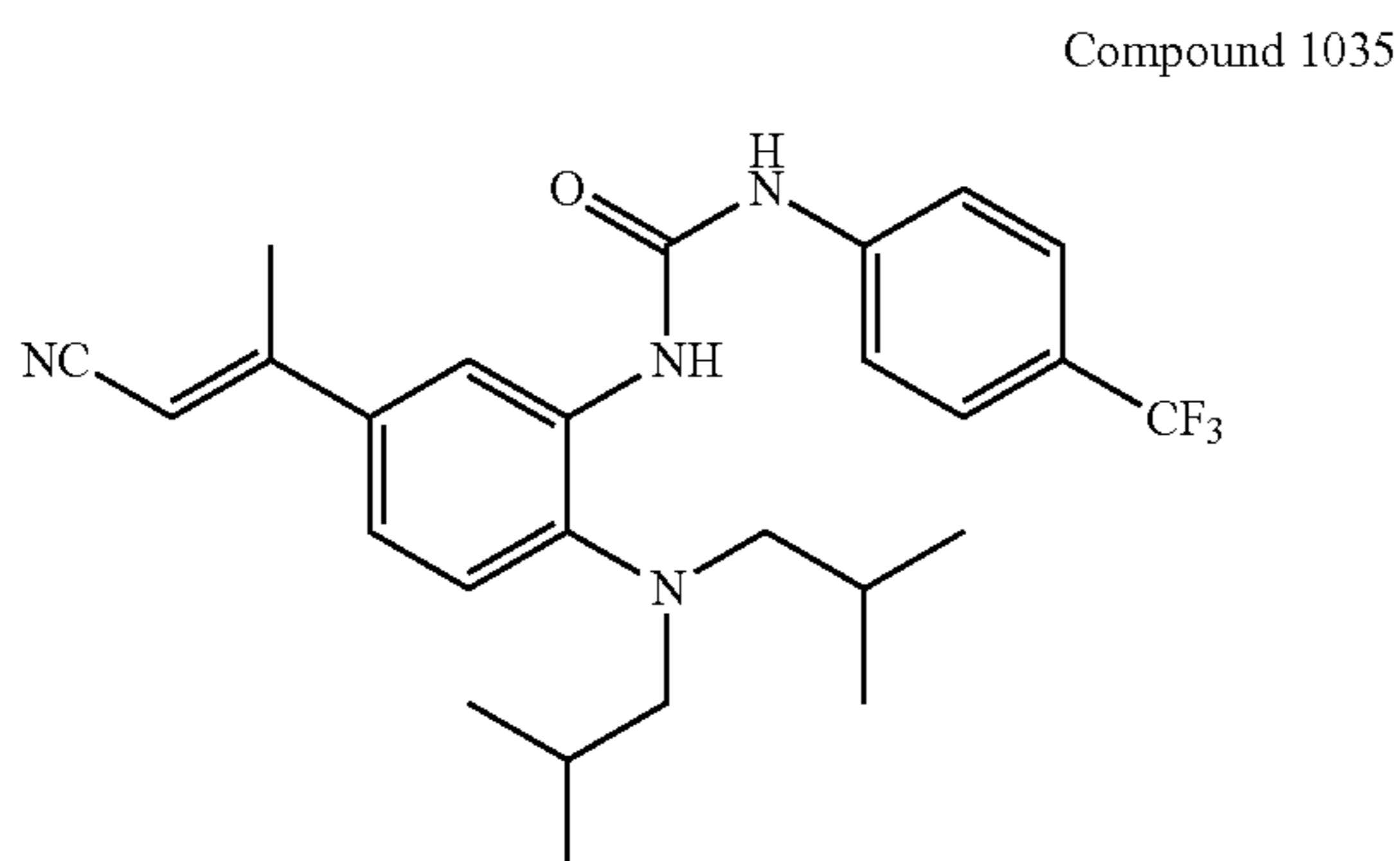
2H), 8.46 (s, 1H), 8.97 (s, 1H), 8.97 (s, 1H), 10.37 (s, 1H), 12.03 (s, 1H). MS (ESI), m/z (%): 440.27[M+H]⁺. White solid.



¹H-NMR (600 MHz, CDCl₃) δ (ppm): 8.37 (d, J=1.8 Hz, 1H), 8.13 (s, 1H), 7.60 (d, J=2.4 Hz, 1H), 7.38 (d, J=8.7 Hz, 1H), 7.27 (dd, J=9.5, 3.1 Hz, 1H), 7.18 (d, J=8.4 Hz, 1H), 7.12 (dd, J=8.3, 2.0 Hz, 1H), 6.48 (s, 1H), 5.64 (s, 1H), 2.62 (d, J=7.2 Hz, 4H), 2.46 (s, 3H), 1.73 (dp, J=13.4, 6.7 Hz, 2H), 0.90 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 474.31 [M+H]⁺. White solid.



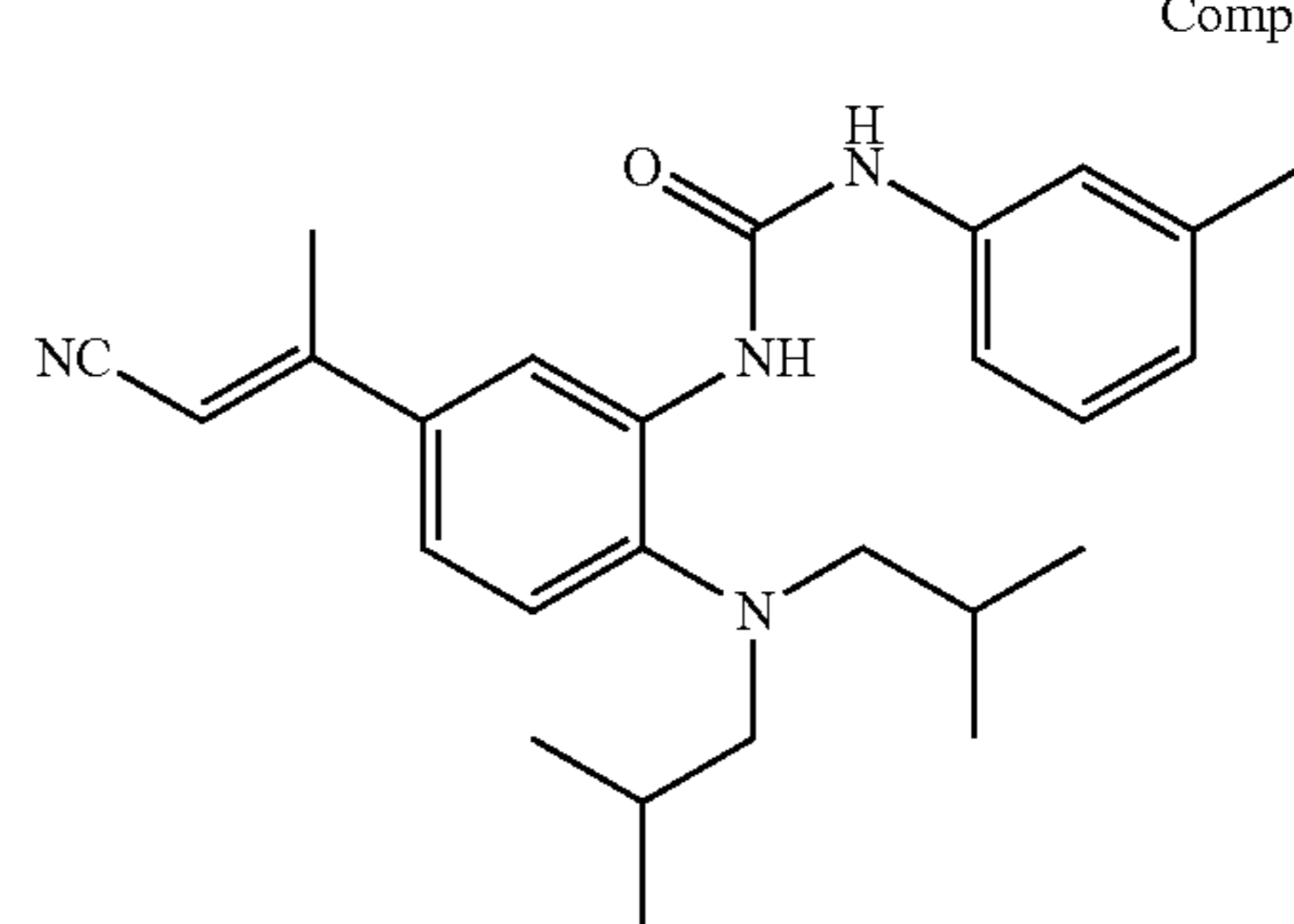
¹H-NMR (600 MHz, CDCl₃) δ (ppm): 8.39 (d, J=1.8 Hz, 1H), 8.15 (s, 1H), 7.66 (d, J=9.8 Hz, 2H), 7.46 (t, J=7.8 Hz, 1H), 7.36 (d, J=7.7 Hz, 1H), 7.19 (d, J=8.3 Hz, 1H), 7.12 (dd, J=8.3, 2.0 Hz, 1H), 6.54 (s, 1H), 5.65 (s, 1H), 2.62 (d, J=7.2 Hz, 4H), 2.46 (s, 3H), 1.83-1.65 (m, 2H), 0.90 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 473.29[M+H]⁺. White solid.



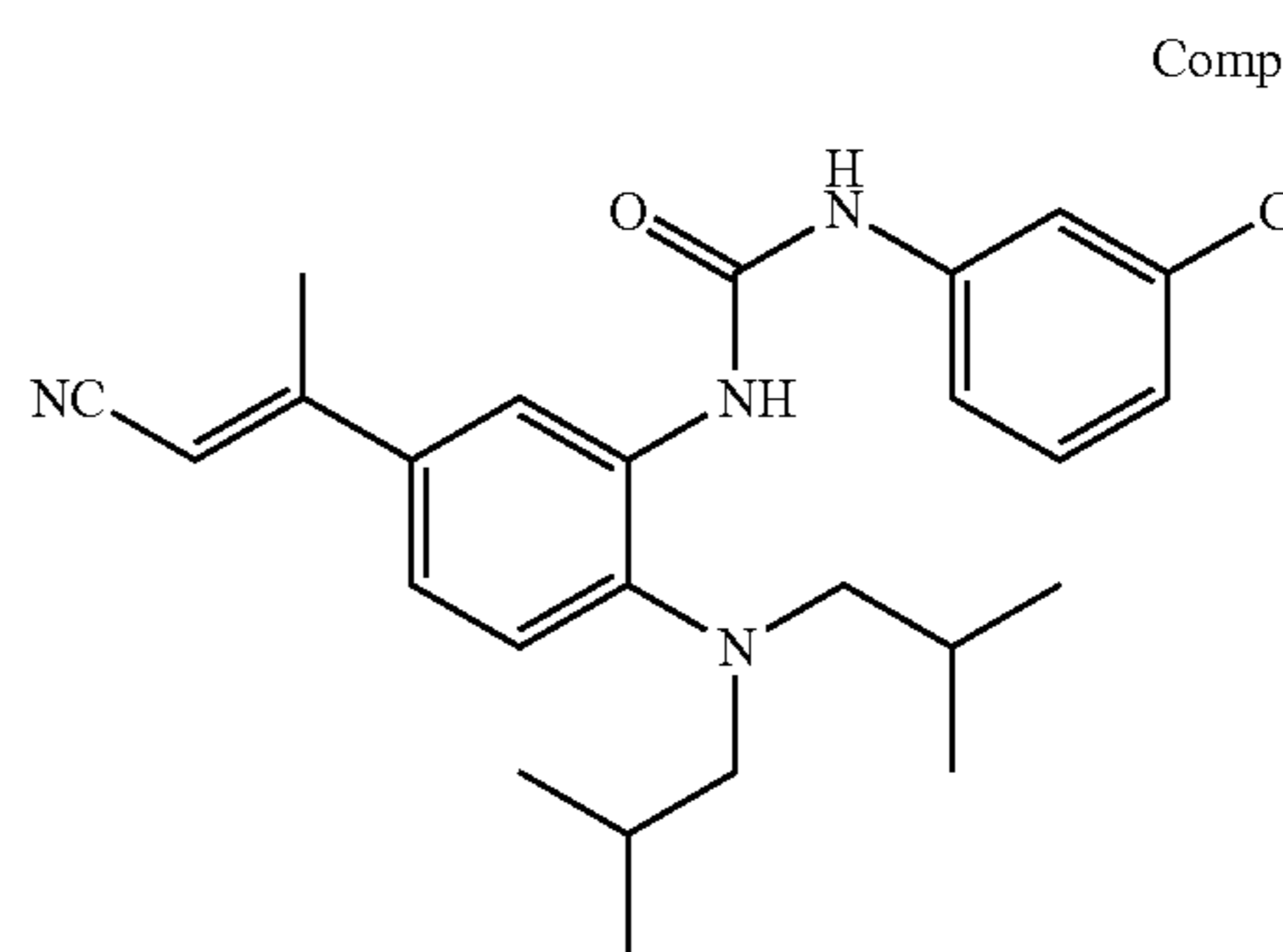
¹H-NMR (600 MHz, CDCl₃) δ (ppm): 8.38 (d, J=1.7 Hz, 1H), 8.17 (s, 1H), 7.66-7.48 (m, 4H), 7.19 (d, J=8.4 Hz, 1H),

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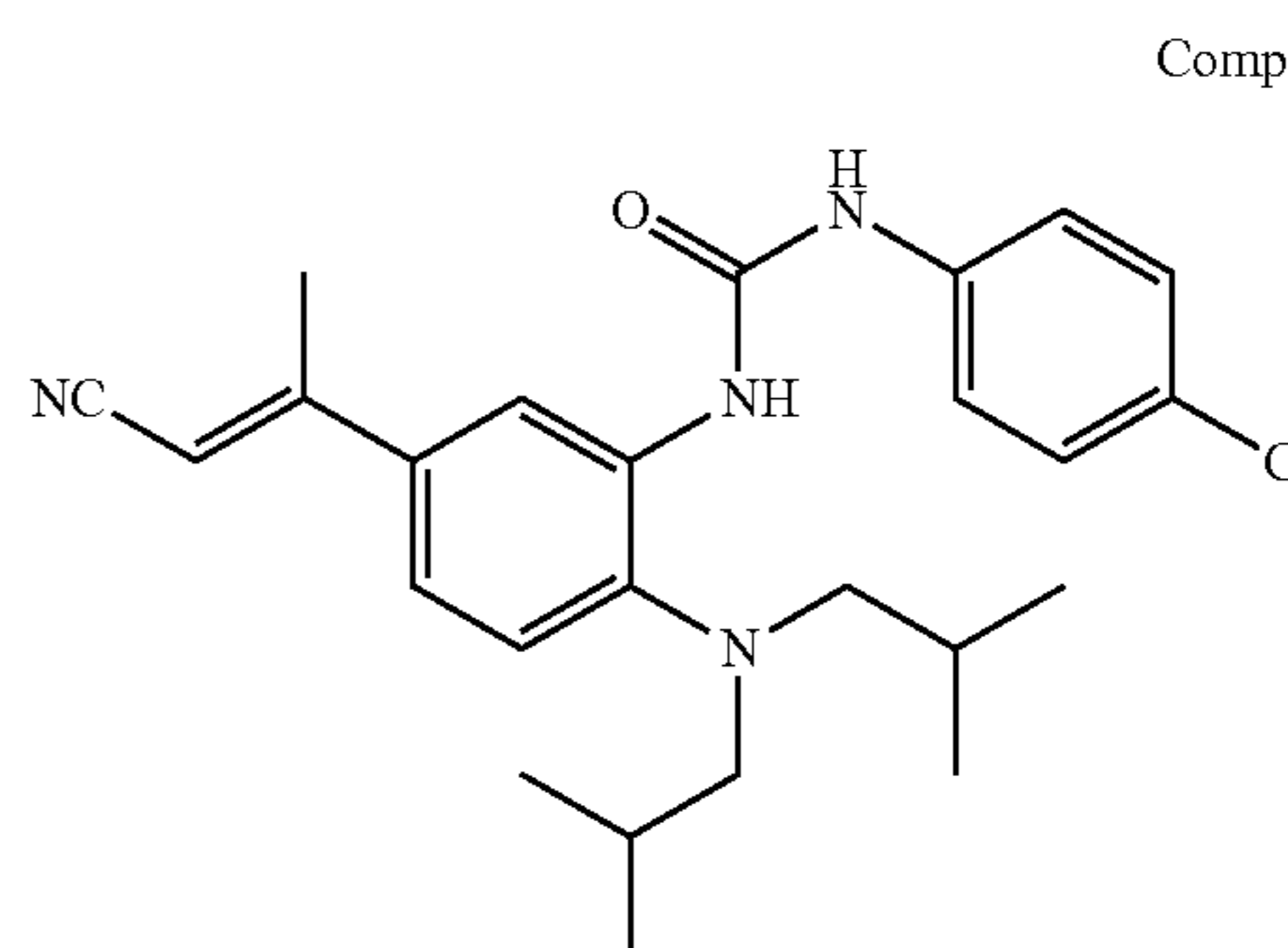
7.13 (dd, J=8.3, 1.8 Hz, 1H), 6.67 (s, 1H), 5.65 (s, 1H), 2.63 (d, J=7.2 Hz, 4H), 2.46 (s, 2H), 1.75 (dd, J=13.4, 6.7 Hz, 2H), 0.91 (d, J=6.5 Hz, 12H). MS (ESI), m/z (%): 473.23 [M+H]⁺. White solid.



¹H-NMR (600 MHz, CDCl₃) δ (ppm): 8.43 (s, 1H), 8.03 (s, 1H), 7.29-7.17 (m, 2H), 7.14 (d, J=8.5 Hz, 2H), 7.09 (d, J=8.3 Hz, 1H), 6.97 (d, J=7.5 Hz, 1H), 6.40 (s, 1H), 5.64 (s, 1H), 2.57 (d, J=7.2 Hz, 4H), 2.46 (s, 3H), 2.35 (s, 3H), 1.68 (m, 2H), 0.83 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 419.35[M+H]⁺. White solid.



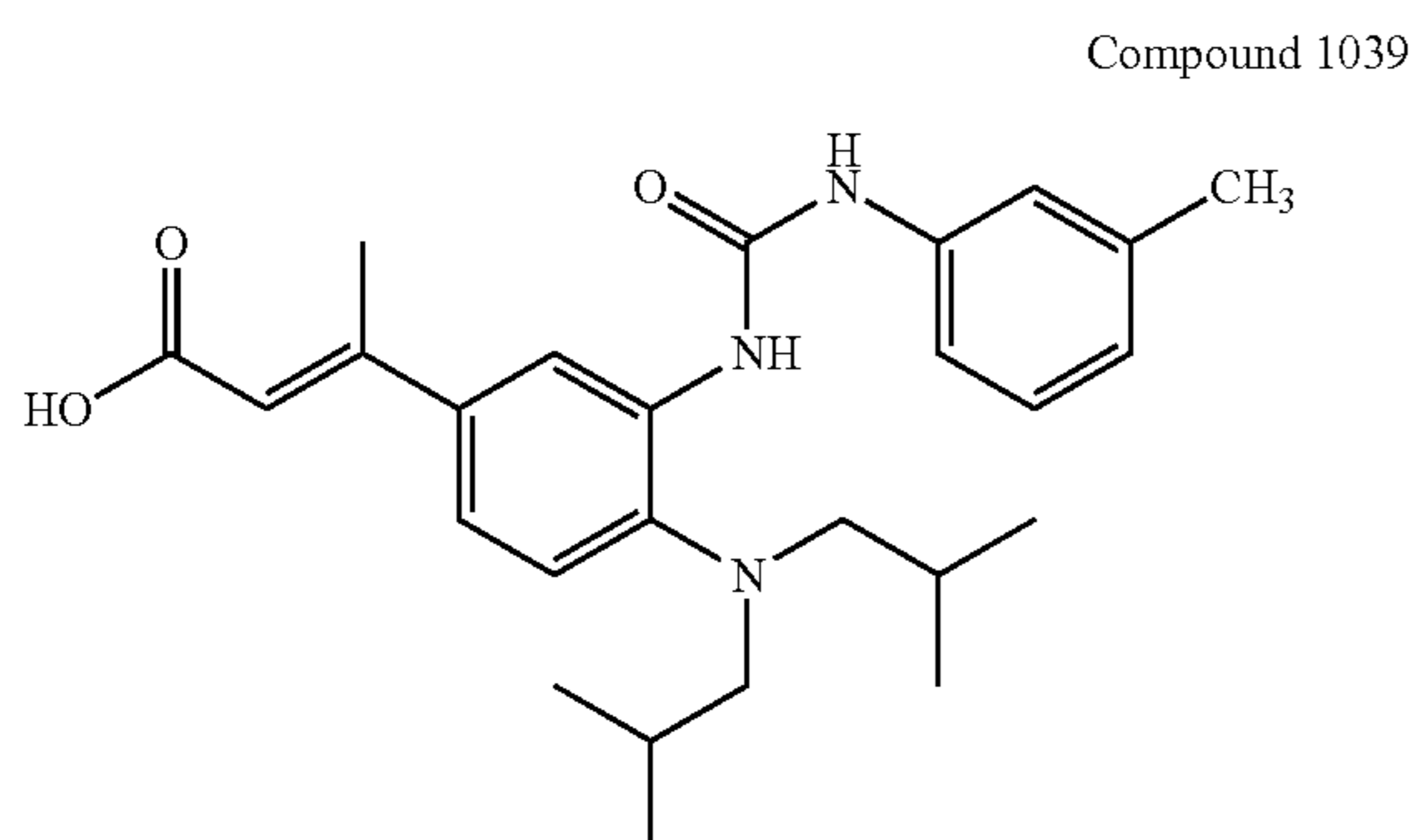
¹H-NMR (600 MHz, CDCl₃) δ (ppm): 8.39 (d, J=1.8 Hz, 1H), 8.12 (s, 1H), 7.46 (s, 1H), 7.27 (d, J=5.6 Hz, 2H), 7.17 (d, J=8.3 Hz, 1H), 7.11 (d, J=7.8 Hz, 2H), 6.41 (s, 1H), 5.64 (s, 1H), 2.60 (d, J=7.2 Hz, 4H), 2.46 (s, 3H), 1.72 (m, 2H), 0.88 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 440.27[M+H]⁺. White solid.



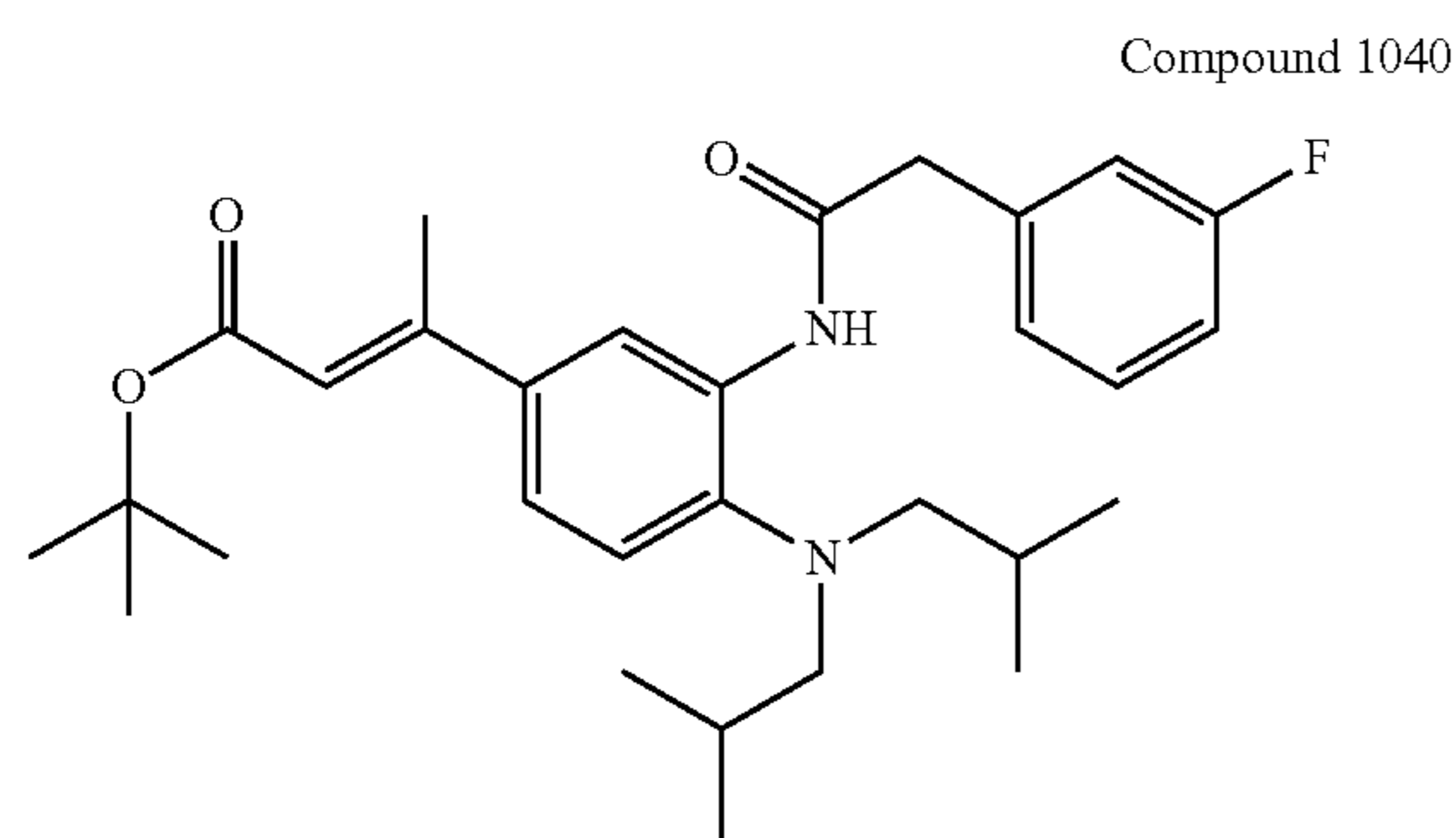
¹H-NMR (600 MHz, CDCl₃) δ (ppm): 8.39 (s, 1H), 8.09 (s, 1H), 7.32 (dd, J=25.8, 8.0 Hz, 4H), 7.17 (d, J=8.3 Hz, 1H), 7.11 (d, J=8.3 Hz, 1H), 6.40 (s, 1H), 5.64 (s, 1H), 2.59

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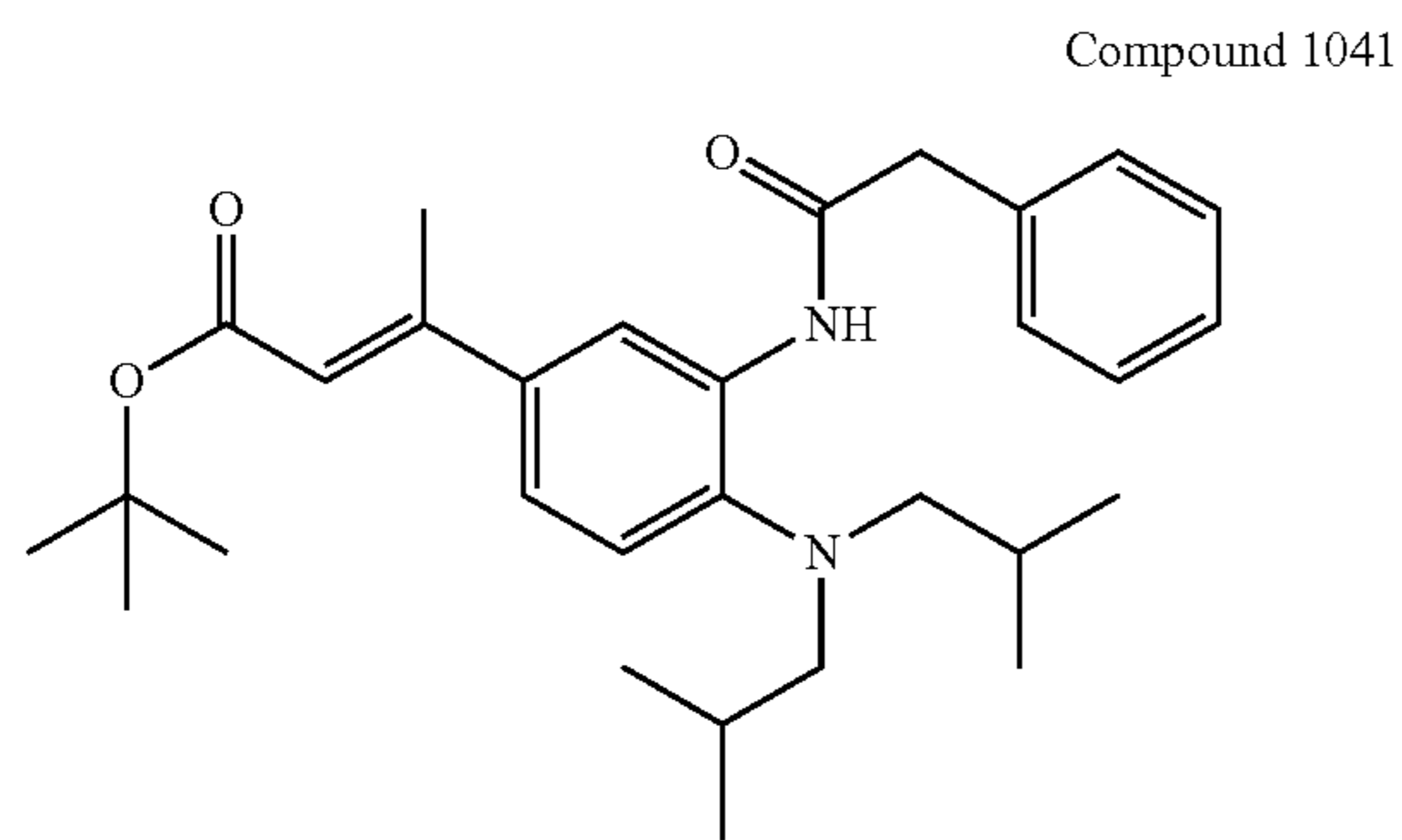
(d, J=6.9 Hz, 4H), 2.46 (s, 3H), 1.81-1.64 (m, 2H), 0.88 (d, J=6.3 Hz, 12H). MS (ESI), m/z (%): 440.27[M+H]⁺. White solid.



¹H-NMR (600 MHz, DMSO-d₆) δ (ppm): 12.13 (s, 1H), 9.42 (s, 1H), 8.16 (d, J=1.9 Hz, 1H), 7.80 (s, 1H), 7.35 (s, 1H), 7.21 (ddd, J=22.3, 20.0, 7.9 Hz, 4H), 6.80 (d, J=7.4 Hz, 1H), 6.07 (s, 1H), 2.74 (d, J=6.9 Hz, 4H), 2.48 (s, 3H), 2.29 (s, 3H), 1.68 (m, 2H), 0.90-0.78 (m, 12H). MS (ESI), m/z (%): 438.30[M+H]⁺. White solid.



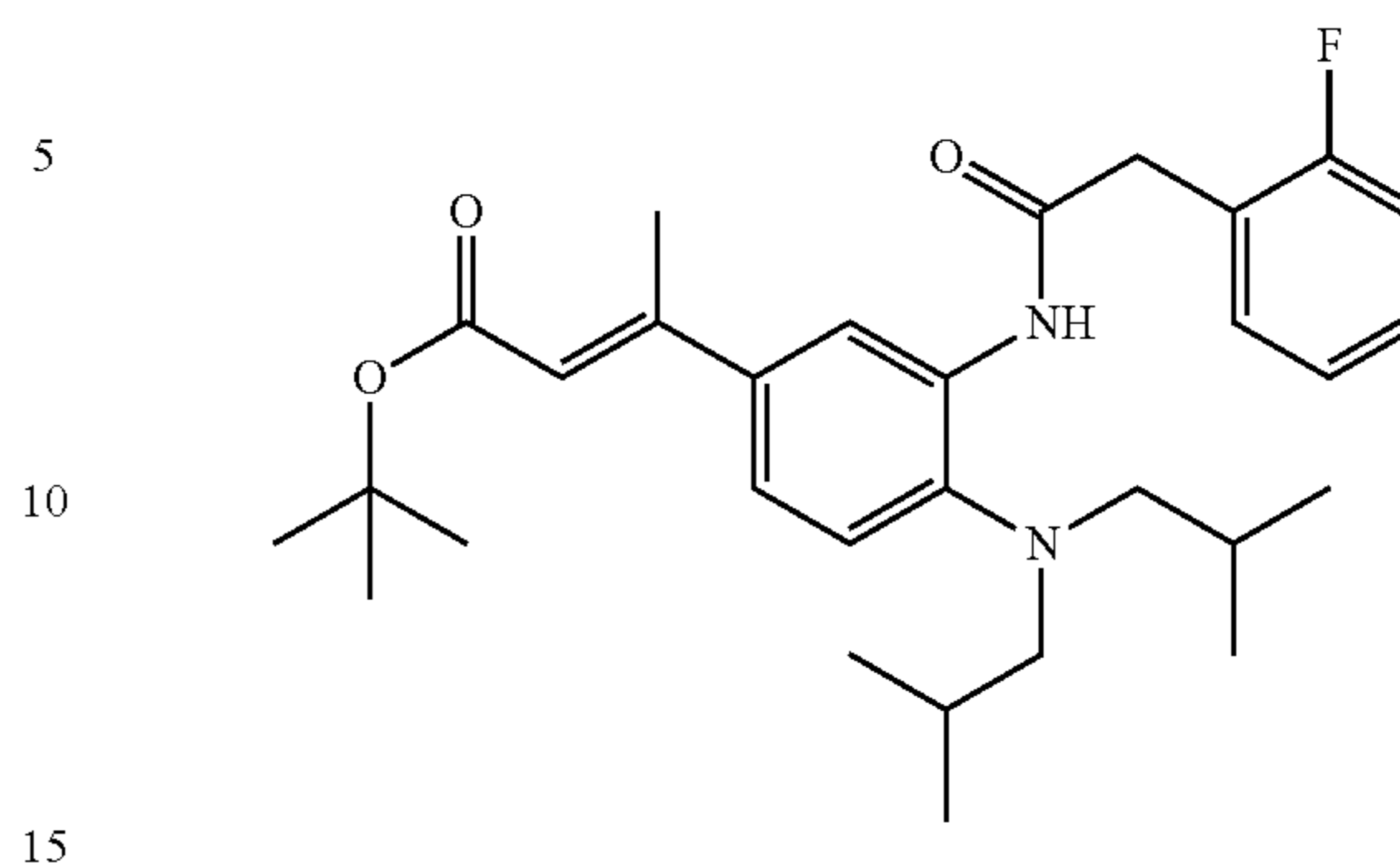
¹H-NMR (400 MHz, DMSO-d₆) δ 8.66 (s, 1H), 8.24 (s, 1H), 7.33 (dd, J=8.3, 5.7 Hz, 2H), 7.24-7.18 (m, 2H), 7.13 (t, J=8.9 Hz, 2H), 5.91 (d, J=1.1 Hz, 1H), 3.71 (s, 2H), 2.54 (t, J=10.5 Hz, 4H), 2.39 (d, J=0.9 Hz, 3H), 1.55 (dt, J=13.2, 6.4 Hz, 2H), 1.42 (s, 9H), 0.73 (t, J=6.6 Hz, 12H). MS (ESI), m/z (%): 497.39 [M+H]⁺. White solid.



¹H-NMR (600 MHz, DMSO-d₆) δ 8.71 (d, J=34.7 Hz, 1H), 8.31 (s, 1H), 7.38-7.31 (m, 4H), 7.28 (t, J=6.4 Hz, 1H), 7.24 (d, J=8.3 Hz, 2H), 5.95 (d, J=1.2 Hz, 1H), 3.73 (d, J=22.4 Hz, 2H), 2.64-2.53 (m, 4H), 2.43 (d, J=1.0 Hz, 3H), 1.58 (dt, J=13.3, 6.5 Hz, 2H), 1.46 (s, 9H), 0.76 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 479.37 [M+H]⁺. White solid.

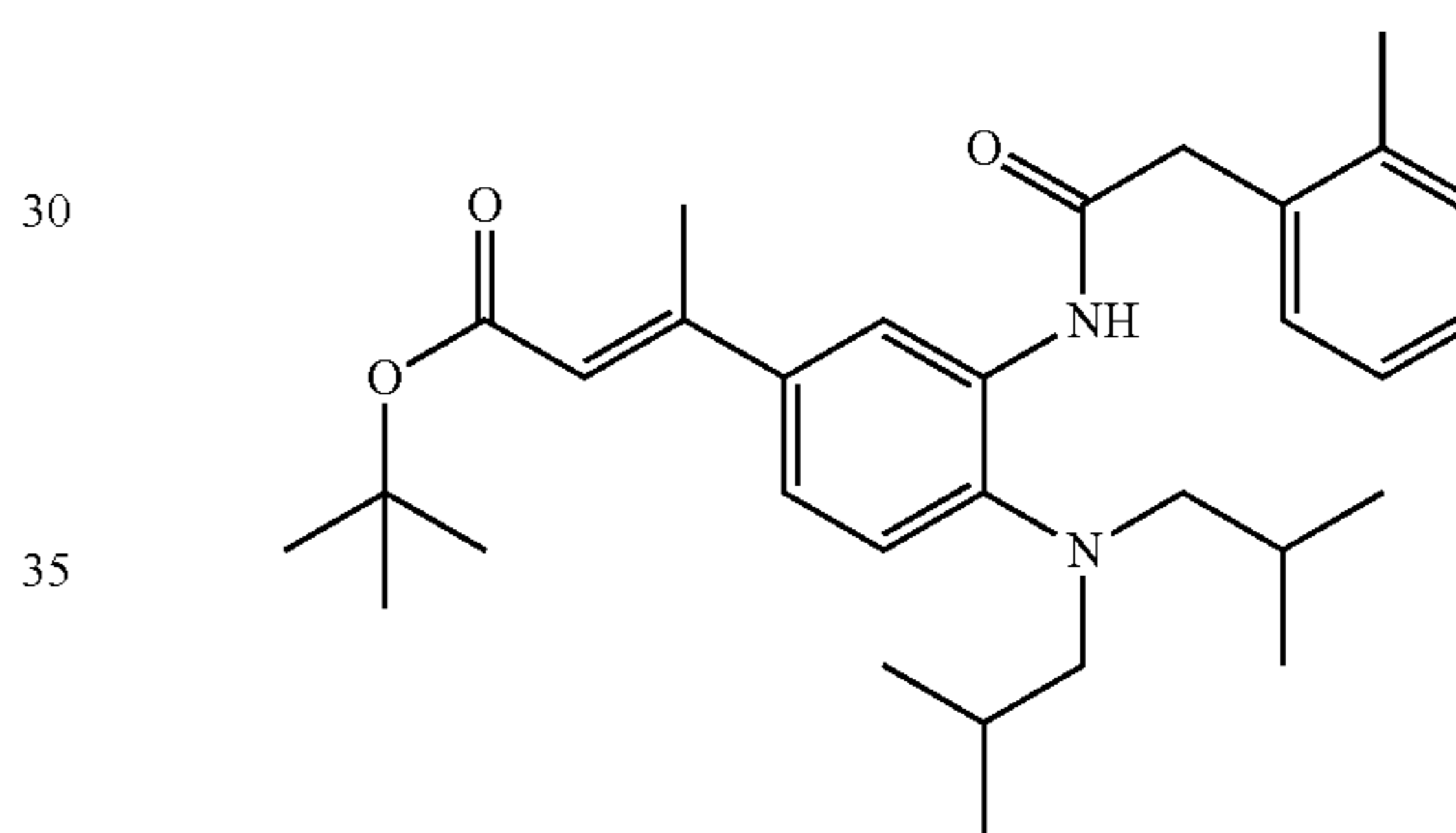
72

Compound 1042



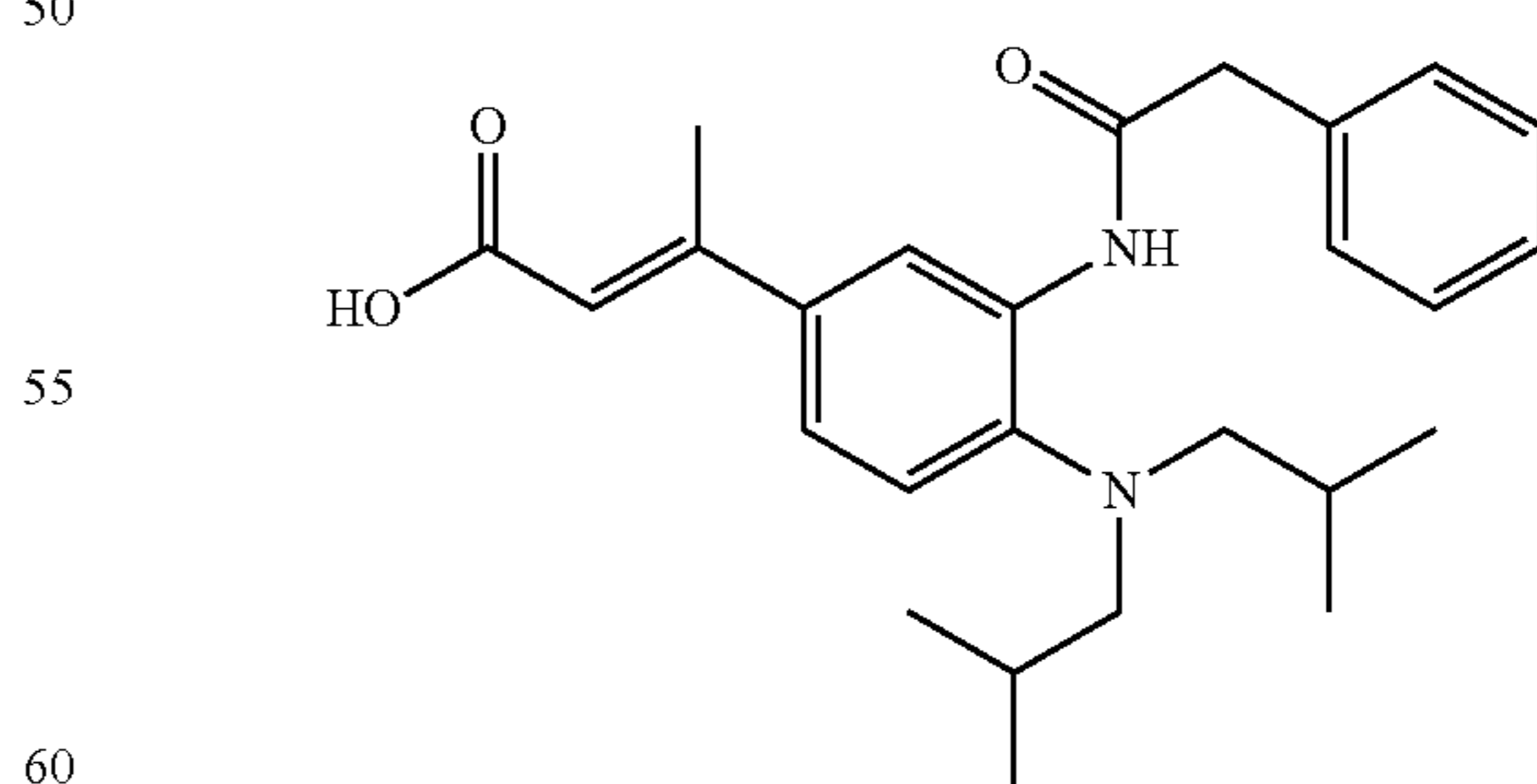
¹H-NMR (600 MHz, DMSO-d₆) 8.79 (d, J=17.0 Hz, 1H), 8.30 (s, 1H), 7.43 (t, J=7.5 Hz, 1H), 7.35 (dd, J=13.8, 7.1 Hz, 1H), 7.27 (s, 2H), 7.20 (dd, J=12.8, 5.9 Hz, 2H), 5.95 (d, J=1.2 Hz, 1H), 3.78 (d, J=25.1 Hz, 2H), 2.59 (dd, J=35.8, 6.6 Hz, 4H), 2.44 (d, J=1.1 Hz, 3H), 1.65-1.56 (nm, 2H), 1.46 (s, 9H), 0.80 (t, J=6.2 Hz, 12H). MS (ESI), m/z (%): 497.39 [M+H]⁺. White solid.

Compound 1043



¹H-NMR (600 MHz, DMSO-d₆) δ 8.48 (s, 1H), 8.38 (s, 1H), 7.32-7.08 (m, 6H), 5.96 (s, 1H), 3.76 (d, J=21.2 Hz, 2H), 2.53 (t, J=9.0 Hz, 4H), 2.44 (s, 3H), 2.25 (d, J=12.5 Hz, 3H), 1.56 (td, J=13.1, 6.5 Hz, 2H), 1.46 (s, 9H), 0.73 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 493.41 [M+H]⁺. White solid.

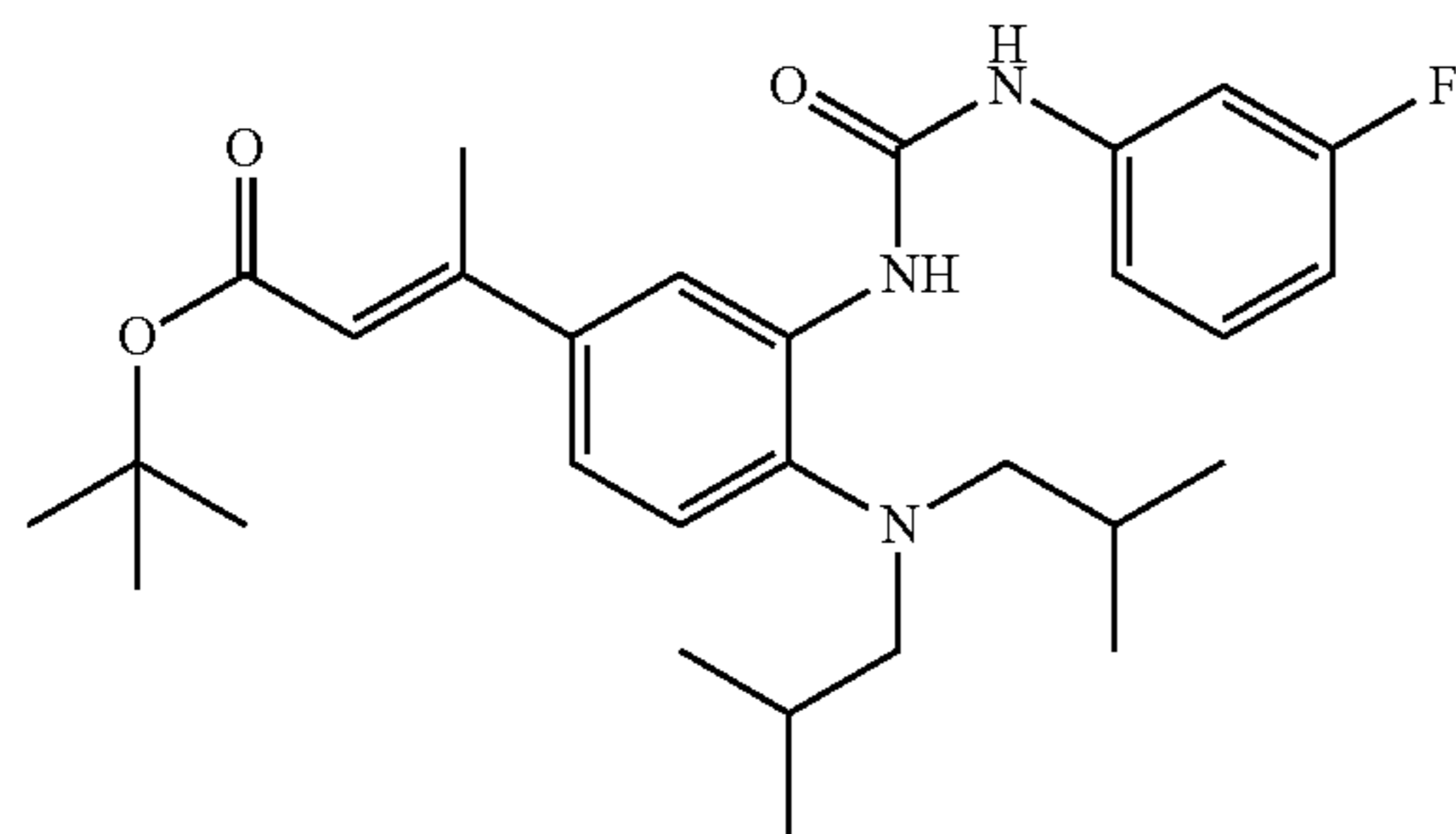
Compound 1044



¹H-NMR (600 MHz, DMSO-d₆) δ 12.14 (s, 1H), 8.71 (d, J=28.8 Hz, 1H), 8.33 (s, 1H), 7.39-7.18 (m, 7H), 6.04 (s, 1H), 3.73 (d, J=19.9 Hz, 2H), 2.56 (dd, J=29.0, 6.8 Hz, 4H), 2.45 (s, 3H), 1.67-1.48 (m, 2H), 0.77 (t, J=9.6 Hz, 12H). MS (ESI), m/z (%): 423.28 [M+H]⁺. White solid.

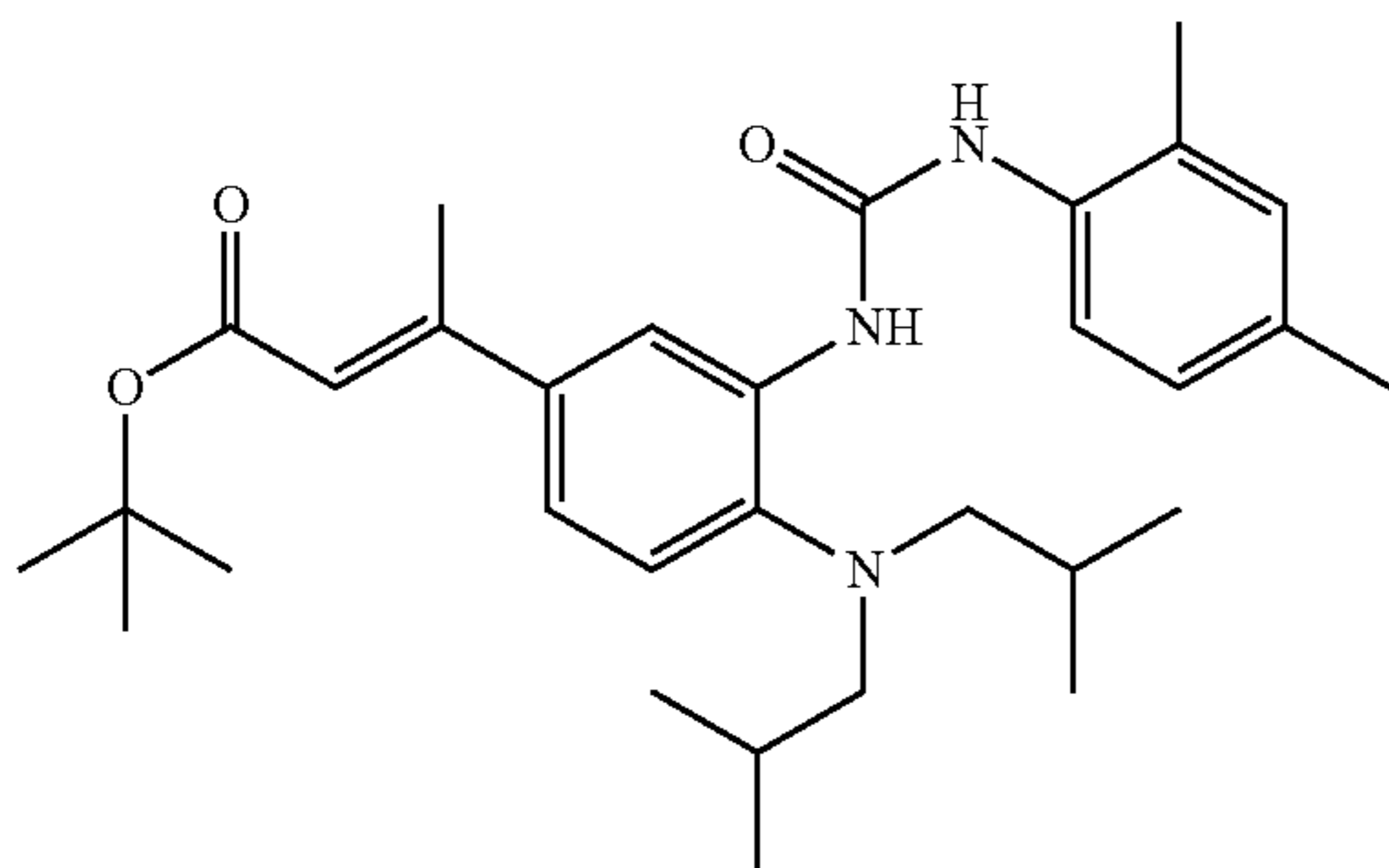
73

Compound 1045



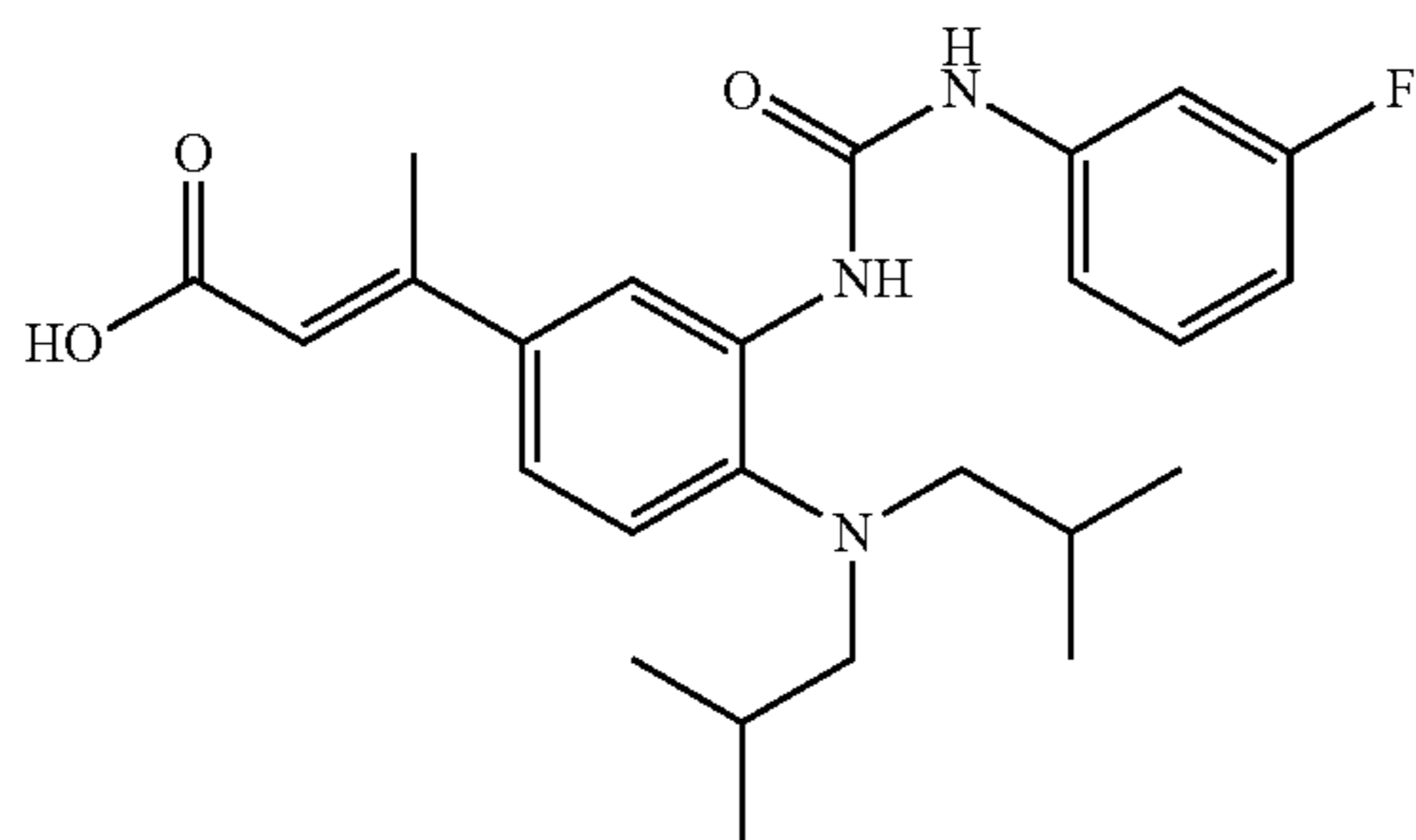
¹H-NMR (400 MHz, DMSO-d₆) δ 9.69 (s, 1H), 8.06 (d, J=1.7 Hz, 1H), 7.82 (s, 1H), 7.48 (d, J=12.0 Hz, 1H), 7.28 (dd, J=15.2, 8.1 Hz, 1H), 7.15 (ddd, J=16.2, 14.1, 8.2 Hz, 3H), 6.80-6.72 (m, 1H), 5.94 (s, 1H), 2.69 (t, J=10.2 Hz, 4H), 2.42 (s, 3H), 1.64 (dt, J=13.2, 6.5 Hz, 2H), 1.43 (s, 9H), 0.80 (d, J=6.6 Hz, 12H). MS (ESI), m/z (%): 498.37 [M+H]⁺. White solid.

Compound 1046



¹H-NMR (400 MHz, DMSO-d₆) δ 8.57 (d, J=22.5 Hz, 1H), 8.06 (d, J=2.0 Hz, 1H), 7.72 (d, J=18.3 Hz, 1H), 7.31 (dd, J=28.4, 9.0 Hz, 1H), 7.12 (dt, J=8.4, 5.3 Hz, 2H), 6.98 (s, 1H), 6.93 (d, J=8.1 Hz, 1H), 5.92 (d, J=1.2 Hz, 1H), 2.70-2.56 (m, 4H), 2.43-2.34 (m, 3H), 2.20 (d, J=8.3 Hz, 3H), 2.16 (d, J=8.7 Hz, 3H), 1.60 (td, J=13.2, 6.5 Hz, 2H), 1.47-1.33 (m, 9H), 0.85-0.71 (m, 12H). MS (ESI), m/z (%): 508.41 [M+H]⁺. White solid.

Compound 1047

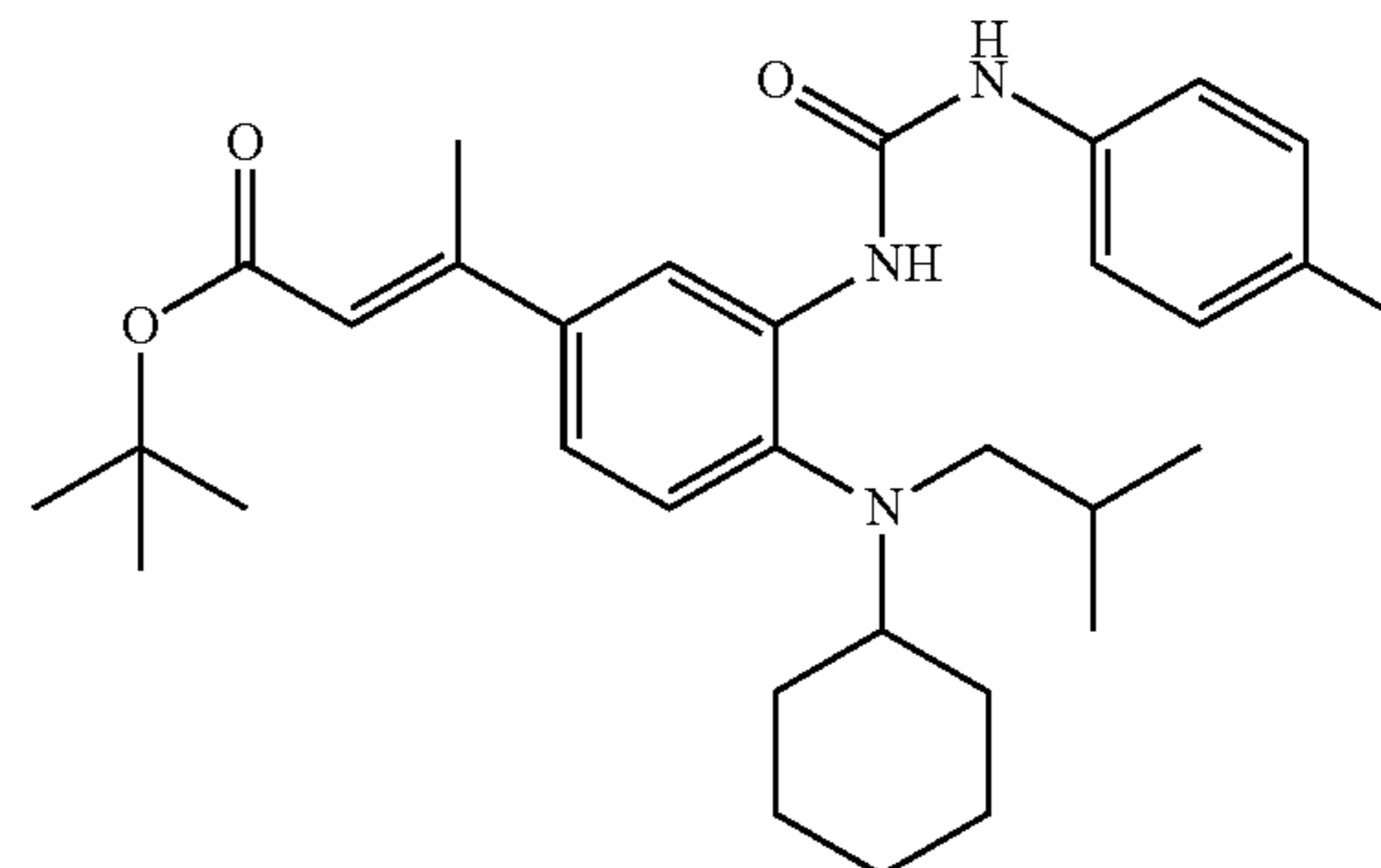


¹H-NMR (400 MHz, DMSO-d₆) δ 9.72 (s, 1H), 8.08 (d, J=2.0 Hz, 1H), 7.84 (s, 1H), 7.49 (d, J=12.0 Hz, 1H), 7.29-7.24 (m, 1H), 7.21-7.15 (m, 2H), 7.11 (d, J=7.9 Hz, 1H), 6.77-6.72 (m, 1H), 6.03 (d, J=1.1 Hz, 1H), 2.71 (d,

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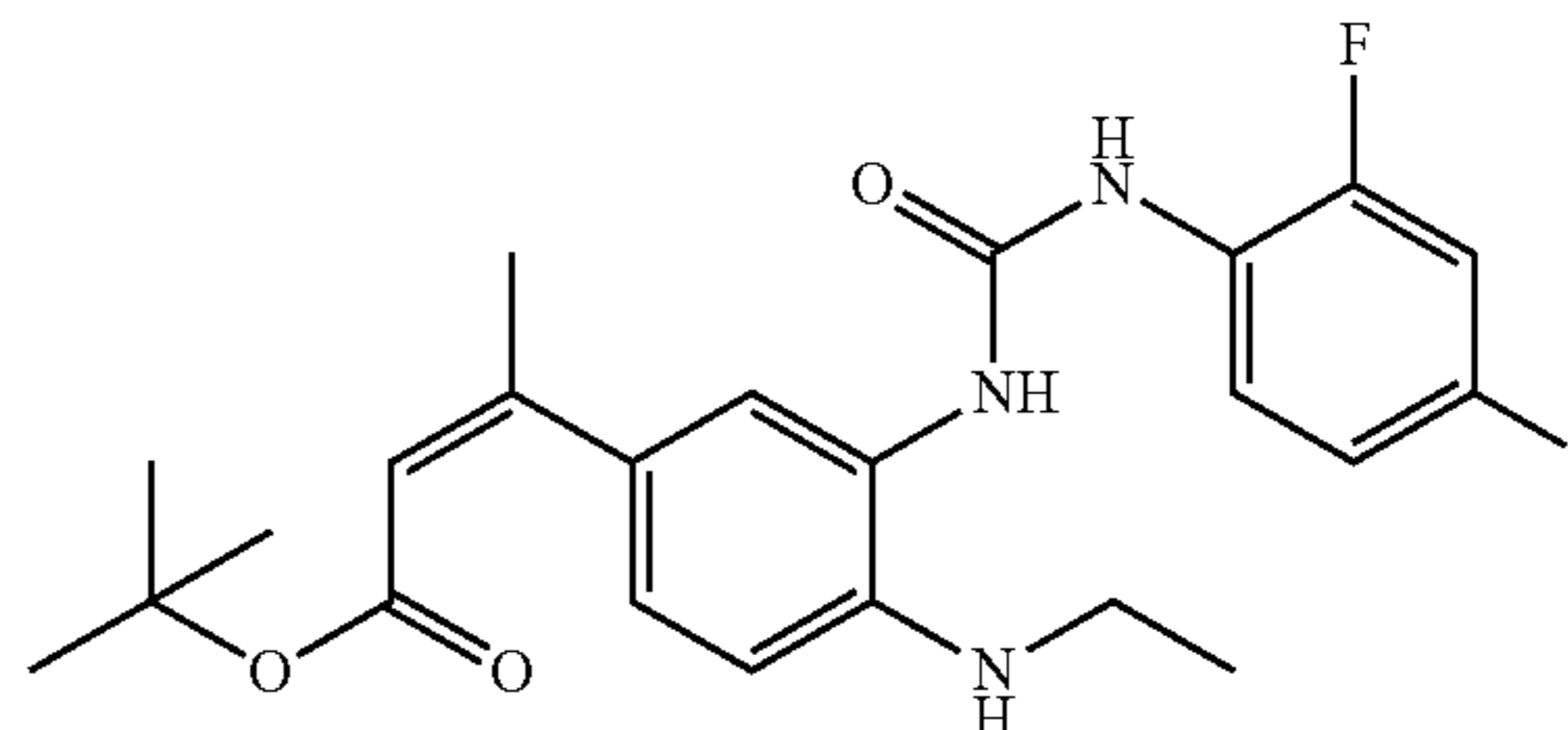
J=6.9 Hz, 4H), 2.43 (s, 3H), 1.64 (dd, J=11.9, 5.4 Hz, 2H), 0.81 (t, J=6.2 Hz, 12H). MS (ESI), m/z (%): 442.29 [M+H]⁺. White solid.

Compound 1048



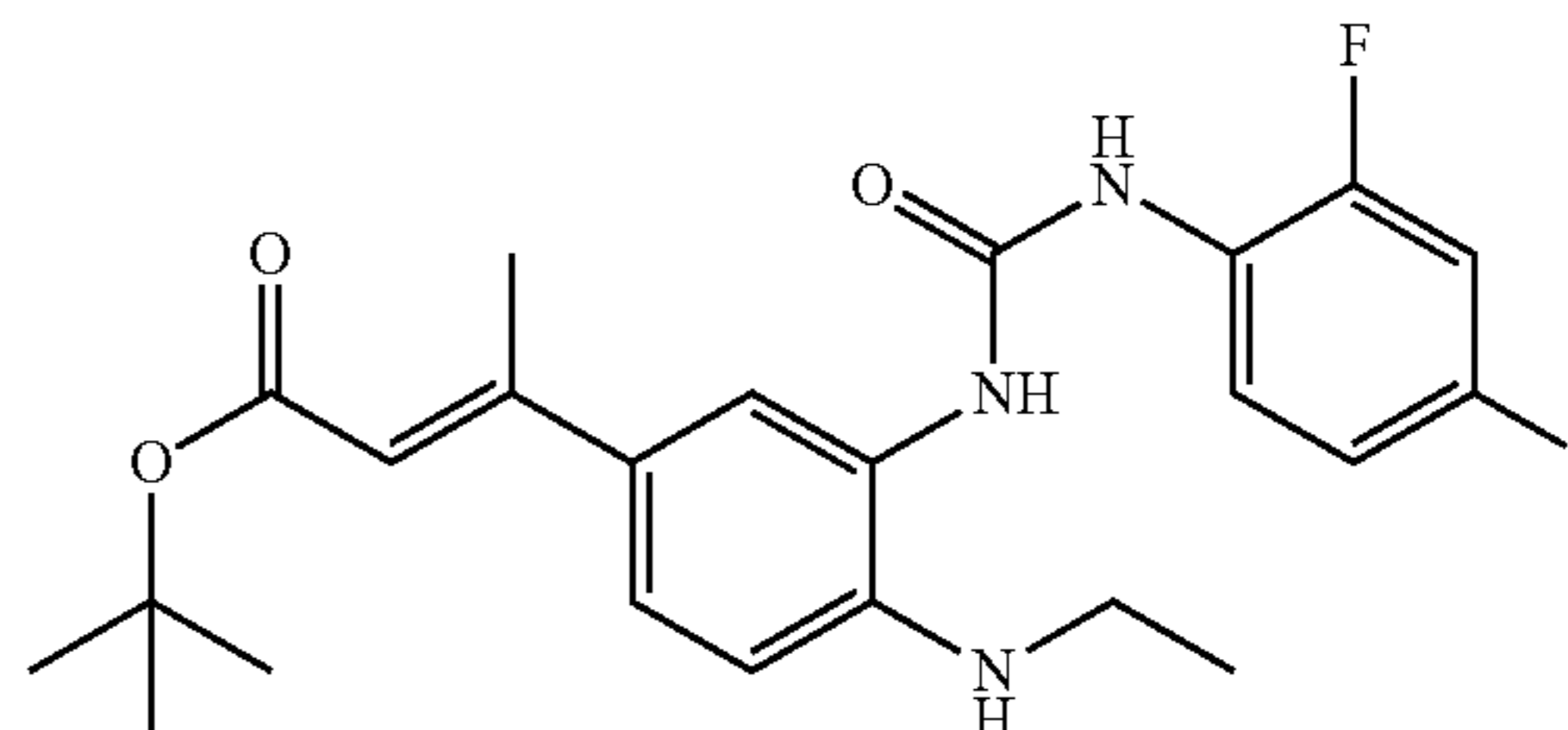
¹H-NMR (500 MHz, DMSO-d₆) δ 9.45 (s, 1H), 8.22 (d, J=2.2 Hz, 1H), 7.91 (s, 1H), 7.36 (dd, J=10.7, 5.5 Hz, 2H), 7.19 (d, J=8.4 Hz, 1H), 7.15 (dd, J=8.3, 2.2 Hz, 1H), 7.10 (d, J=8.3 Hz, 2H), 5.99 (d, J=1.2 Hz, 1H), 2.81 (d, J=5.0 Hz, 2H), 2.58 (dd, J=23.5, 11.8 Hz, 1H), 2.47 (d, J=1.0 Hz, 3H), 2.25 (s, 3H), 1.87 (d, J=11.1 Hz, 2H), 1.69 (d, J=12.5 Hz, 2H), 1.51 (d, J=8.4 Hz, 1H), 1.48 (s, 9H), 1.33 (ddd, J=25.1, 12.5, 5.5 Hz, 2H), 1.29-1.21 (m, 4H), 0.83 (d, J=6.6 Hz, 6H). MS (ESI), m/z (%): 520.40 [M+H]⁺. White solid.

Compound 1049



¹H-NMR (500 MHz, DMSO-d₆) δ 8.89 (s, 2H), 8.04 (td, J=9.1, 6.3 Hz, 1H), 7.68 (d, J=2.2 Hz, 1H), 7.36-7.19 (m, 2H), 7.02 (dd, J=11.4, 4.8 Hz, 1H), 6.87 (d, J=8.5 Hz, 1H), 5.95 (s, 1H), 3.19 (q, J=7.1 Hz, 2H), 2.43 (s, 3H), 1.44 (s, 9H), 1.22 (dd, J=9.1, 5.1 Hz, 3H). MS (ESI), m/z (%): 432.22 [M+H]⁺. White solid.

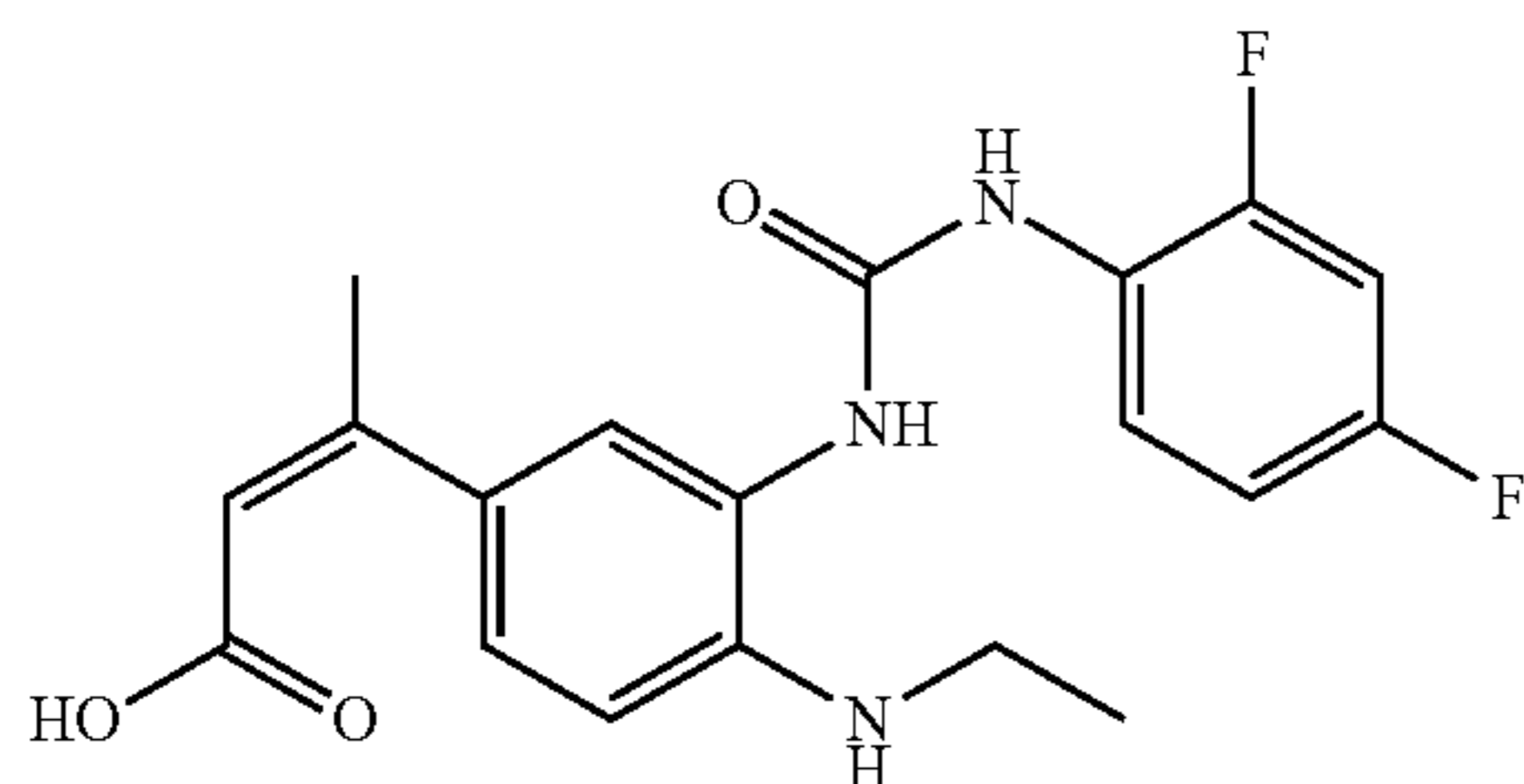
Compound 1050



¹H-NMR (600 MHz, DMSO-d₆) δ 9.40 (s, 1H), 8.71 (s, 11H), 8.53 (s, 1H), 8.20-8.07 (m, 1H), 7.46 (dd, J=15.3, 8.8 Hz, 1H), 7.27 (s, 1H), 7.08-6.96 (m, 2H), 6.05 (s, 1H), 3.28 (d, J=57.3 Hz, 2H), 2.50 (s, 3H), 1.48 (s, 9H), 1.04 (t, J=6.9 Hz, 3H). MS (ESI), m/z (%): 432.23 [M+H]⁺. White solid.

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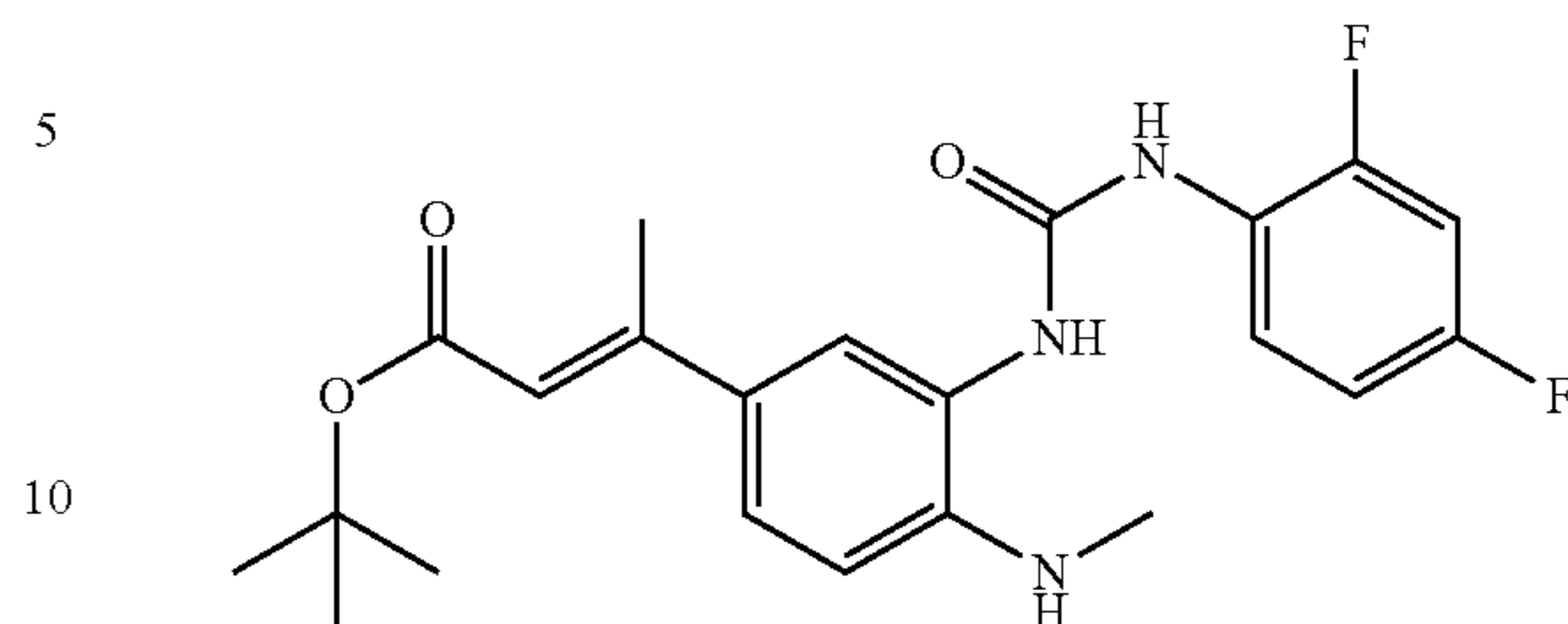
Compound 1051



¹H-NMR (600 MHz, DMSO-d₆) δ 11.88 (s, 1H), 8.63 (s, 1H), 8.21-8.03 (m, 2H), 7.61 (s, 1H), 7.38-7.22 (m, 2H), 7.00 (dt, J=10.3, 5.5 Hz, 1H), 6.66 (d, J=8.6 Hz, 1H), 6.01 (s, 1H), 3.14 (t, J=12.4 Hz, 2H), 2.46 (s, 3H), 1.22 (t, J=7.1 Hz, 3H). MS (ESI), m/z (%): 376.16 [M+H]⁺. White solid.

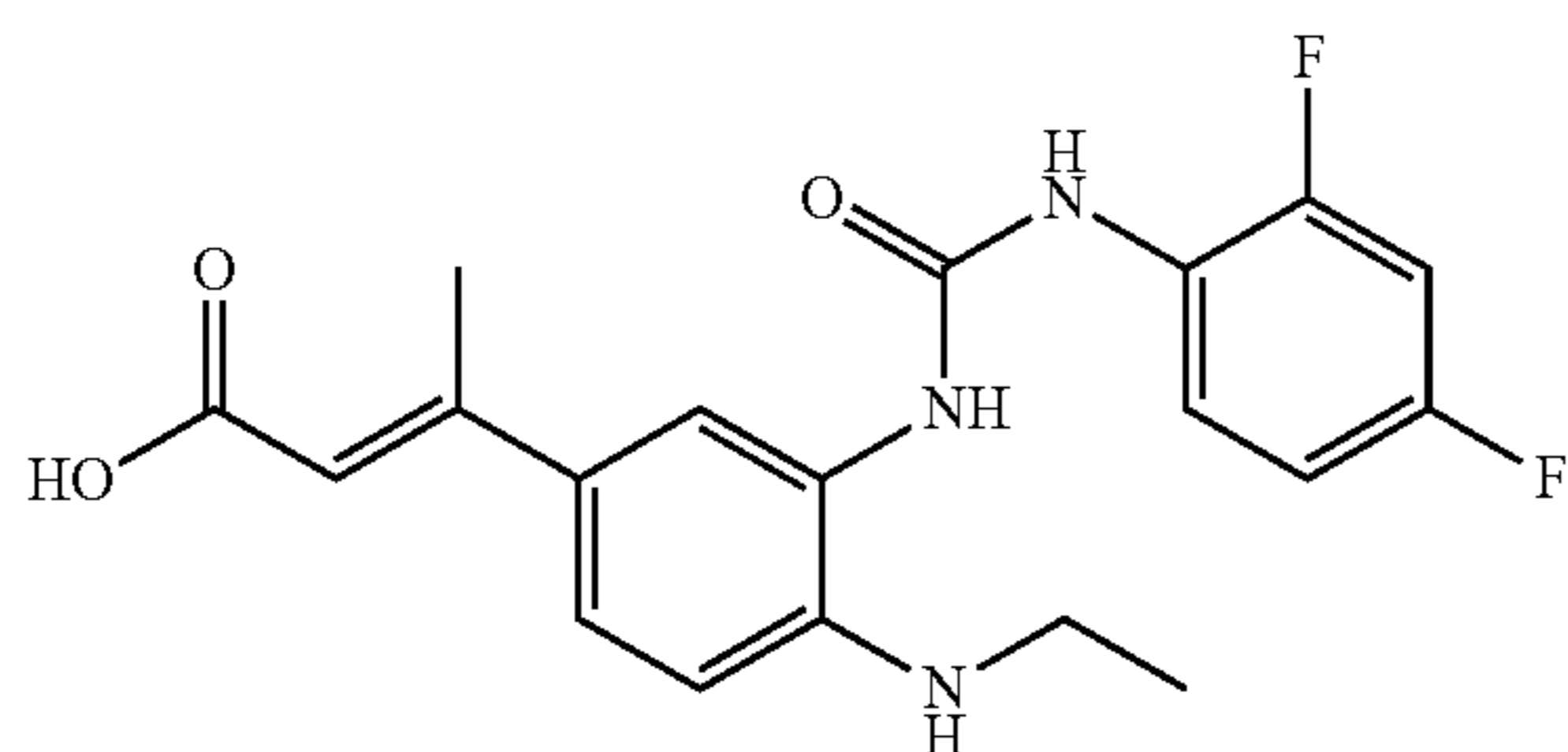
76

Compound 1054



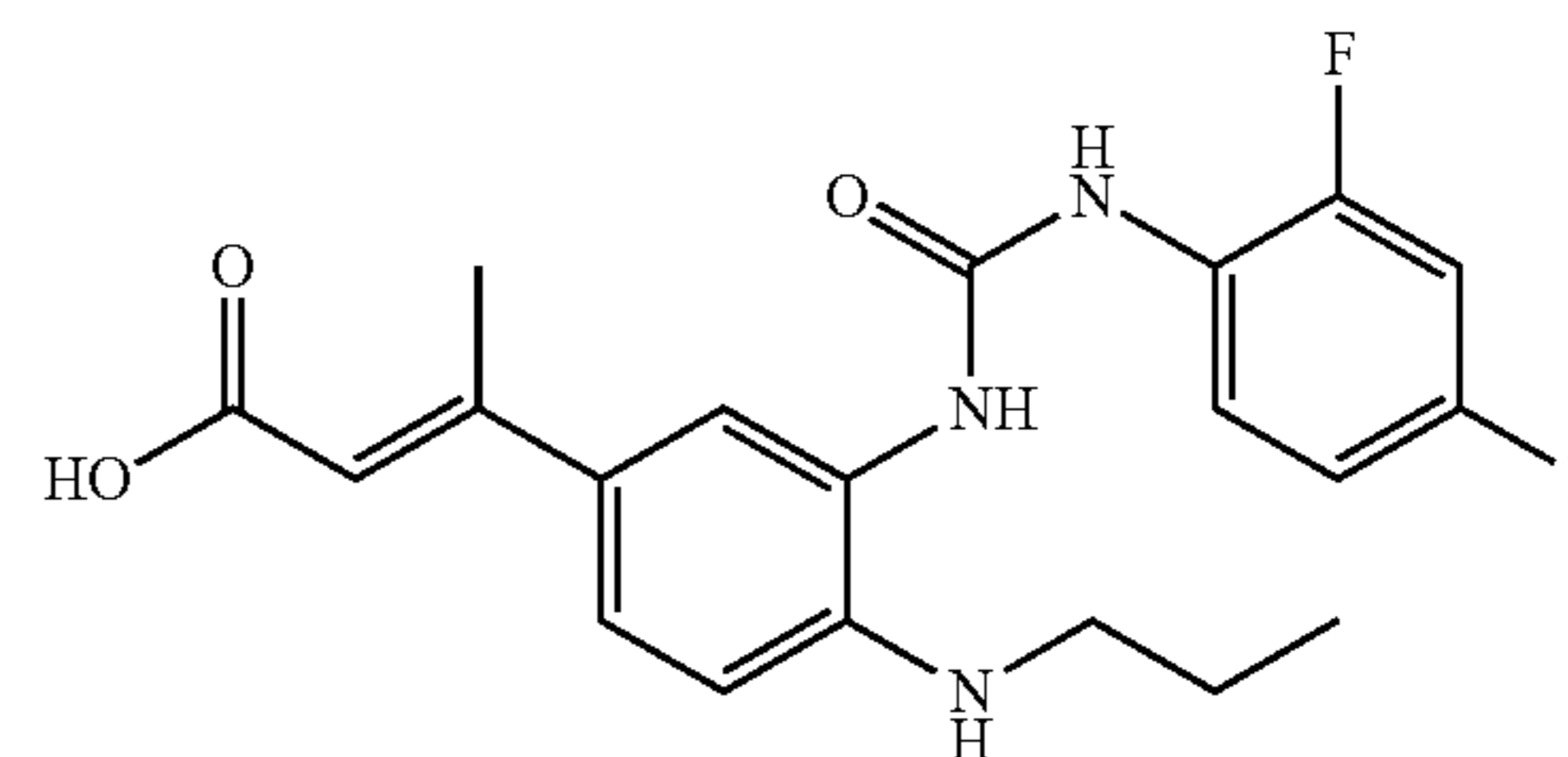
¹H-NMR (400 MHz, DMSO-d₆) δ 9.33 (s, 1H), 8.72 (s, 1H), 8.47 (d, J=2.0 Hz, 1H), 8.12 (td, J=9.3, 6.1 Hz, 1H), 7.69 (s, 1H), 7.27 (s, 1H), 7.03 (d, J=9.2 Hz, 1H), 6.95 (d, J=9.0 Hz, 1H), 6.00 (d, J=1.2 Hz, 1H), 3.07 (s, 3H), 2.45 (d, J=1.1 Hz, 3H), 1.44 (s, 9H). MS (ESI), m/z (%): 418.22 [M+H]⁺. White solid.

Compound 1052



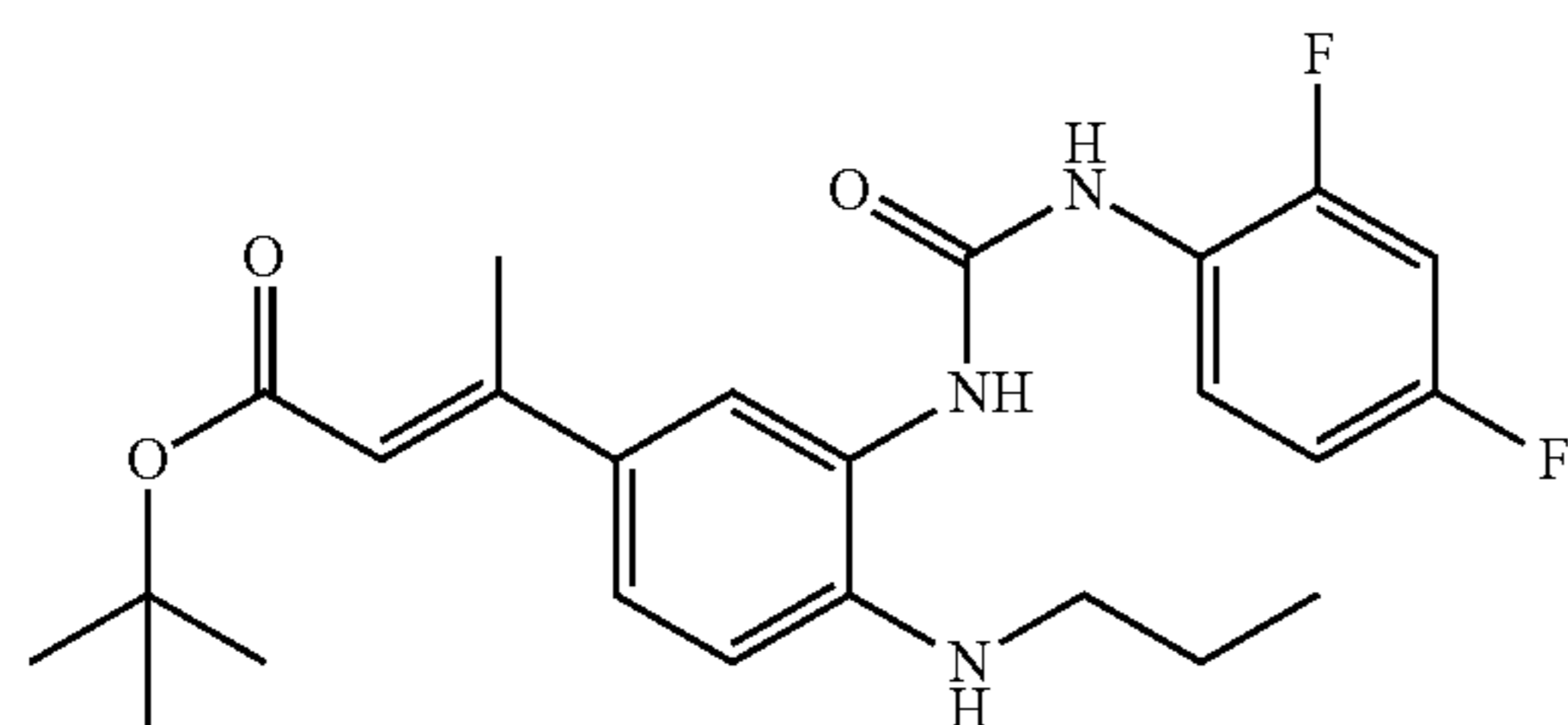
¹H-NMR (600 MHz, DMSO-d₆) δ 12.26 (s, 1H), 9.40 (s, 1H), 8.72 (s, 1H), 8.57 (s, 1H), 8.21-8.10 (m, 1H), 7.54 (d, J=16.3 Hz, 1H), 7.46 (dd, J=15.6, 7.7 Hz, 1H), 7.25-7.17 (m, 1H), 7.01 (ddd, J=22.5, 16.5, 9.2 Hz, 2H), 6.14 (s, 1H), 3.93 (s, 1H), 3.23 (s, 1H), 2.53-2.51 (m, 3H), 1.05 (t, J=7.1 Hz, 3H). MS (ESI), m/z (%): 376.16 [M+H]⁺. White solid.

Compound 1055



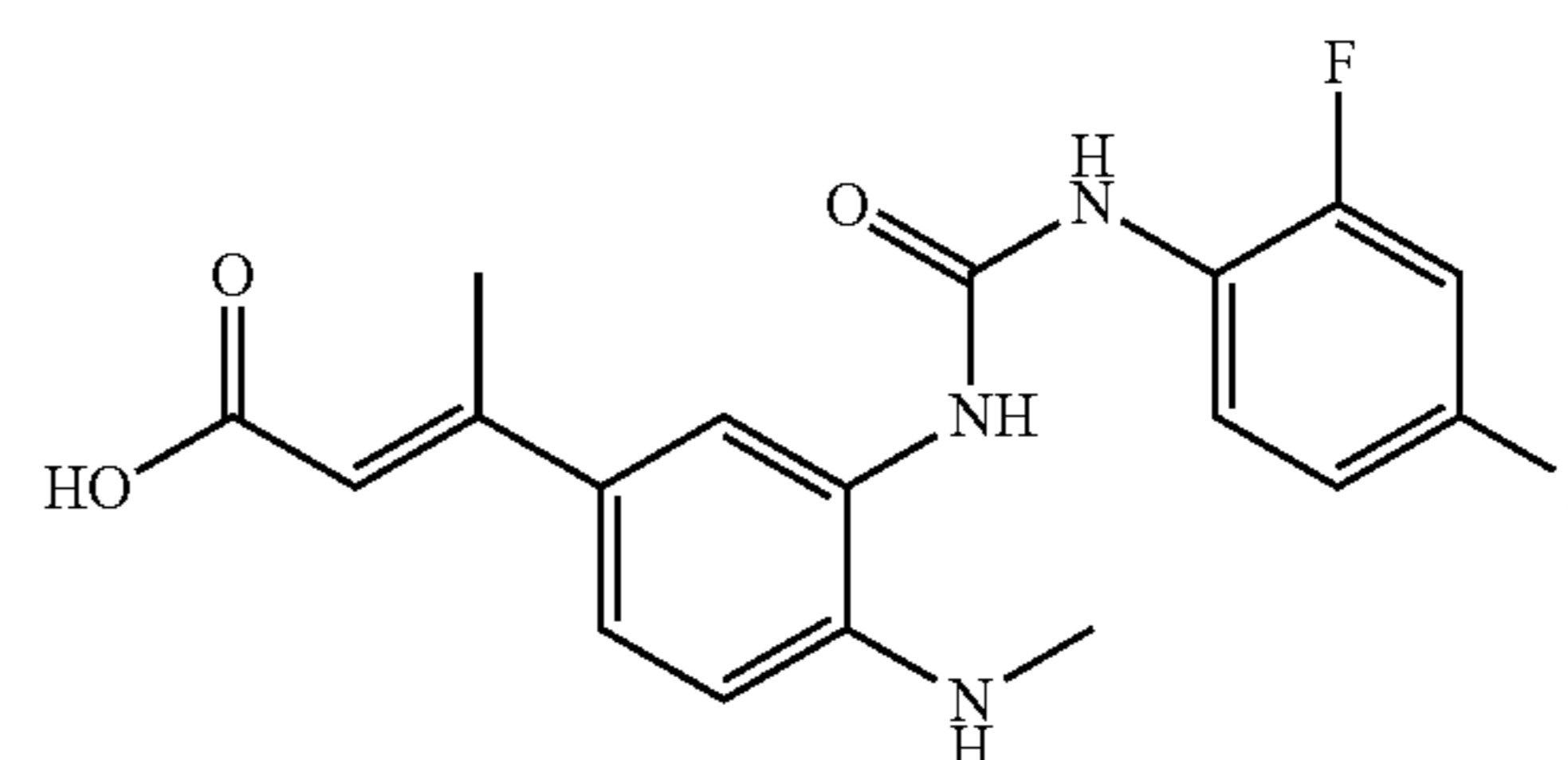
¹H-NMR (600 MHz, DMSO-d₆) δ 12.63-11.42 (m, 1H), 9.24 (s, 1H), 8.83-8.55 (m, 2H), 8.36-8.14 (m, 1H), 7.98 (s, 1H), 7.25 (dd, J=33.2, 25.4 Hz, 2H), 6.88-6.81 (m, 2H), 6.21 (s, 1H), 4.02 (s, 1H), 3.20 (s, 1H), 2.65-2.59 (m, 3H), 1.64 (s, 2H), 0.92 (dd, J=14.9, 7.4 Hz, 3H). MS (ESI), m/z (%): 390.21 [M+H]⁺. White solid.

Compound 1053



¹H-NMR (400 MHz, DMSO-d₆) δ 9.37 (s, 1H), 8.66 (s, 1H), 8.49 (d, J=1.6 Hz, 1H), 8.11 (dd, J=9.2, 3.1 Hz, 1H), 7.50 (s, 1H), 7.40 (dd, J=9.0, 2.7 Hz, 1H), 7.23 (d, J=1.4 Hz, 1H), 7.03 (d, J=9.1 Hz, 1H), 6.95 (d, J=7.7 Hz, 1H), 6.00 (d, J=1.2 Hz, 1H), 3.81 (s, 2H), 3.04 (s, 2H), 2.46 (s, 3H), 1.44 (s, 9H), 0.79 (t, J=7.4 Hz, 3H). MS (ESI), m/z (%): 446.23 [M+H]⁺. White solid.

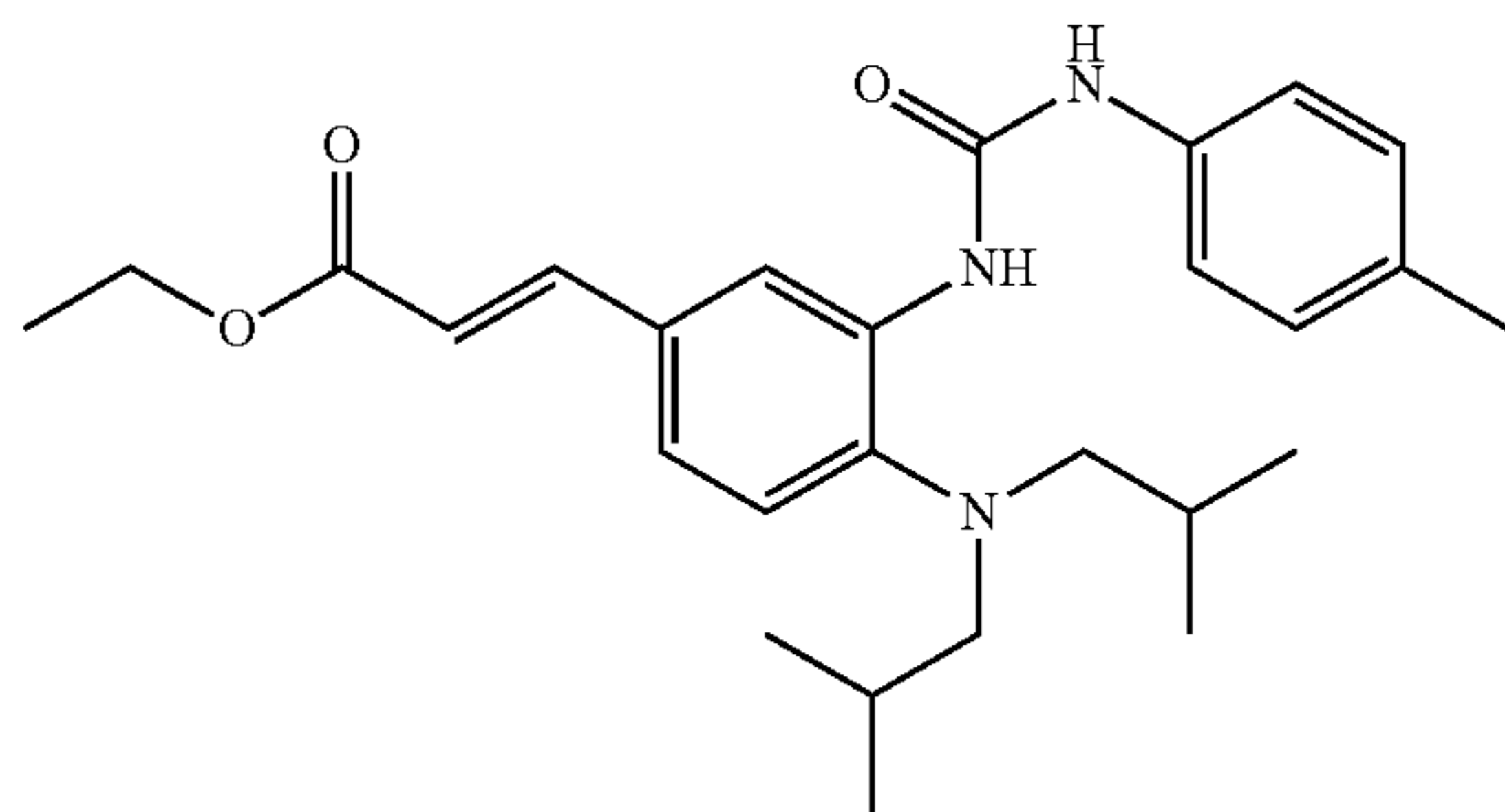
Compound 1056



¹H-NMR (600 MHz, DMSO-d₆) δ 9.17-9.02 (m, 1H), 8.70 (d, J=46.5 Hz, 2H), 8.22 (dd, J=15.1, 9.1 Hz, 1H), 7.96 (s, 1H), 7.30 (s, 2H), 6.86-6.80 (m, 2H), 6.21 (s, 1H), 3.27 (d, J=5.4 Hz, 3H), 2.58 (s, 3H). MS (ESI), m/z (%): 362.26 [M+H]⁺. White solid.

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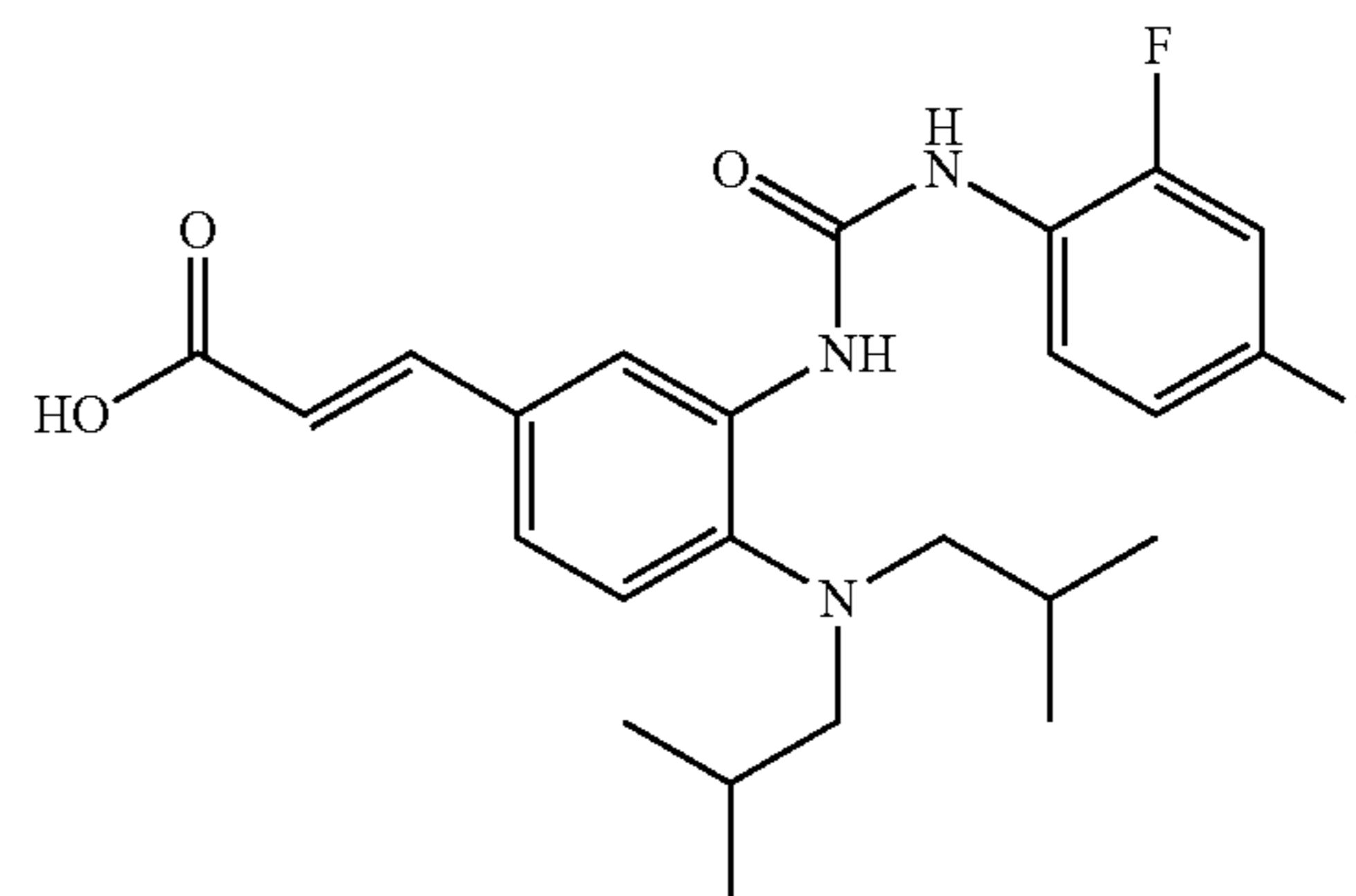
Compound 1057



$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.45 (s, 1H), 7.96 (s, 1H), 7.63 (d, $J=16.0$ Hz, 1H), 7.21 (s, 1H), 7.14 (s, 1H), 7.11 (s, 3H), 6.41 (d, $J=16.0$ Hz, 1H), 4.22 (q, $J=7.1$ Hz, 2H), 2.53 (d, $J=7.2$ Hz, 4H), 2.32 (s, 3H), 1.65 (dt, $J=13.5, 6.7$ Hz, 2H), 1.31 (t, $J=7.1$ Hz, 3H), 0.79 (d, $J=6.6$ Hz, 12H). MS(ESI), m/z (%): 452.34 $[\text{M}+\text{H}]^+$. White solid.

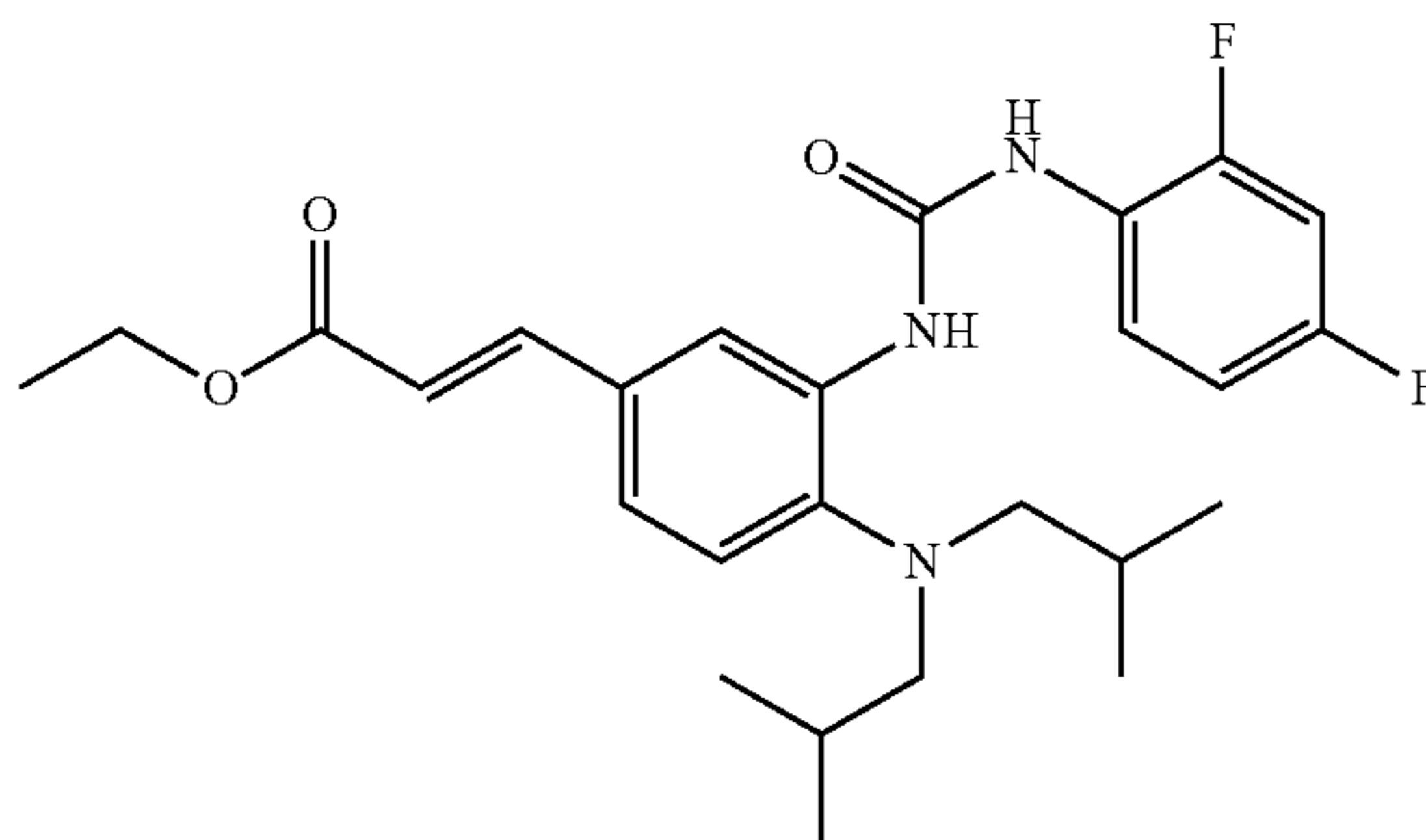
78

Compound 1060



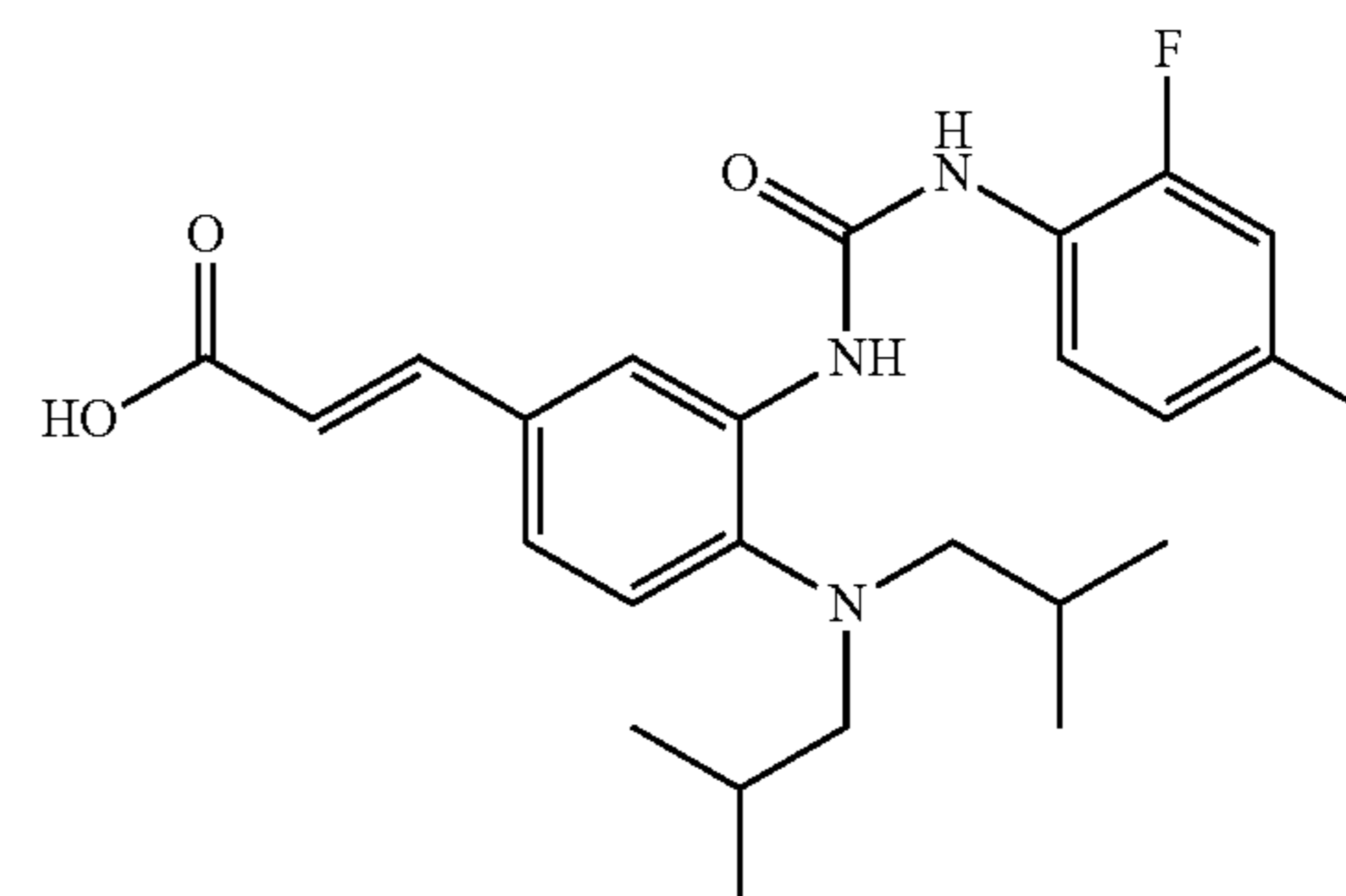
$^1\text{H-NMR}$ (600 MHz, DMSO-d_6) δ 12.28 (s, 1H), 9.33 (s, 1H), 8.05 (d, $J=15.7$ Hz, 3H), 7.49 (d, $J=15.8$ Hz, 1H), 7.30 (d, $J=8.3$ Hz, 2H), 7.20 (s, 1H), 7.05 (s, 1H), 6.34-6.26 (m, 1H), 2.81 (d, $J=6.3$ Hz, 4H), 1.77-1.65 (m, 2H), 0.83 (d, $J=6.1$ Hz, 12H). MS(ESI), m/z (%): 446.23 $[\text{M}+\text{H}]^+$. White solid.

Compound 1058



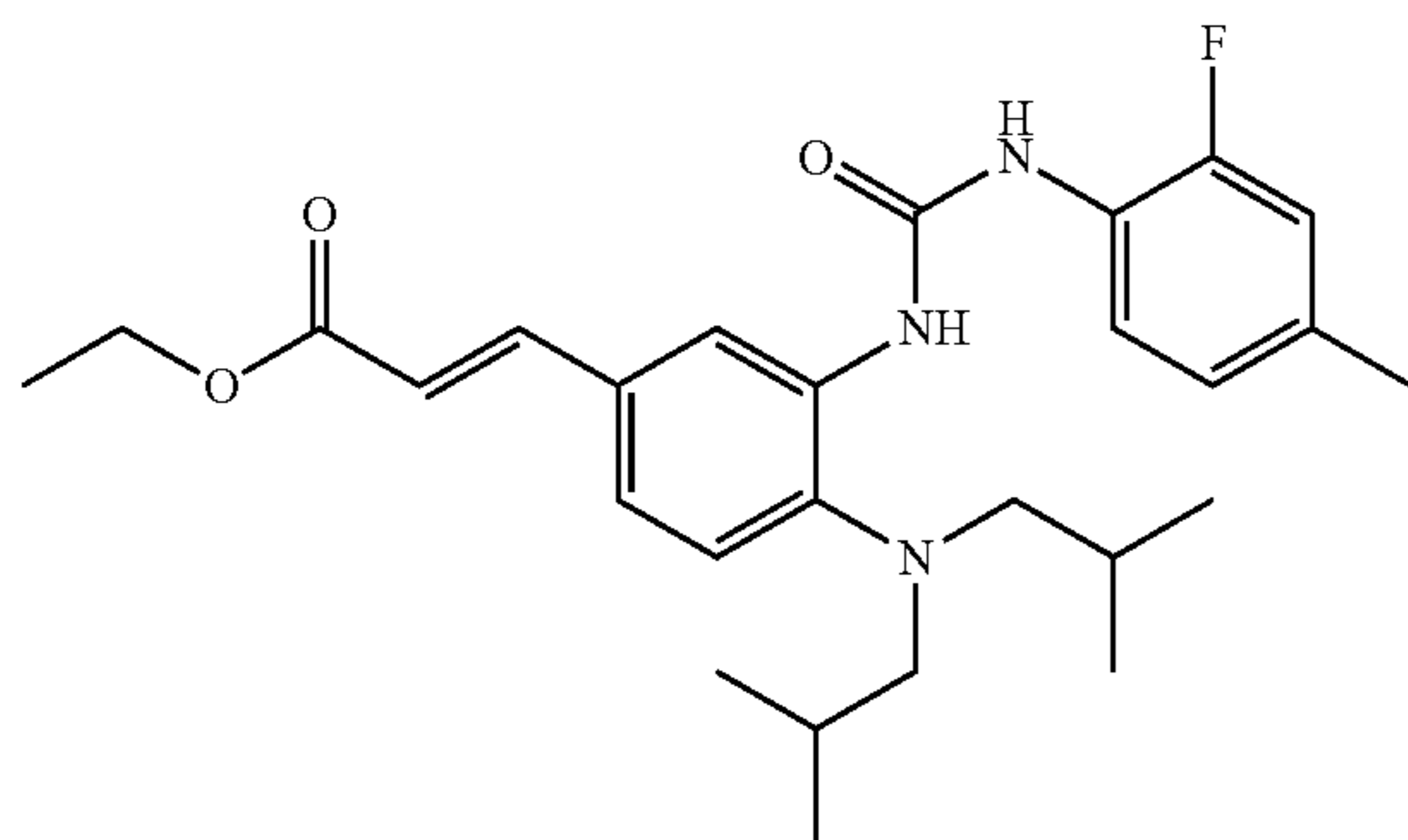
$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.41 (s, 1H), 8.18 (s, 1H), 7.99 (td, $J=9.2, 6.0$ Hz, 1H), 7.63 (d, $J=16.0$ Hz, 1H), 7.14 (s, 2H), 6.90-6.81 (m, 2H), 6.39 (s, 1H), 4.23 (q, $J=7.1$ Hz, 2H), 2.59 (d, $J=7.3$ Hz, 4H), 1.72 (dt, $J=13.5, 6.8$ Hz, 2H), 1.31 (t, $J=7.1$ Hz, 3H), 0.88 (d, $J=6.6$ Hz, 12H). MS(ESI), m/z (%): 474.33 $[\text{M}+\text{H}]^+$. White solid.

Compound 1061



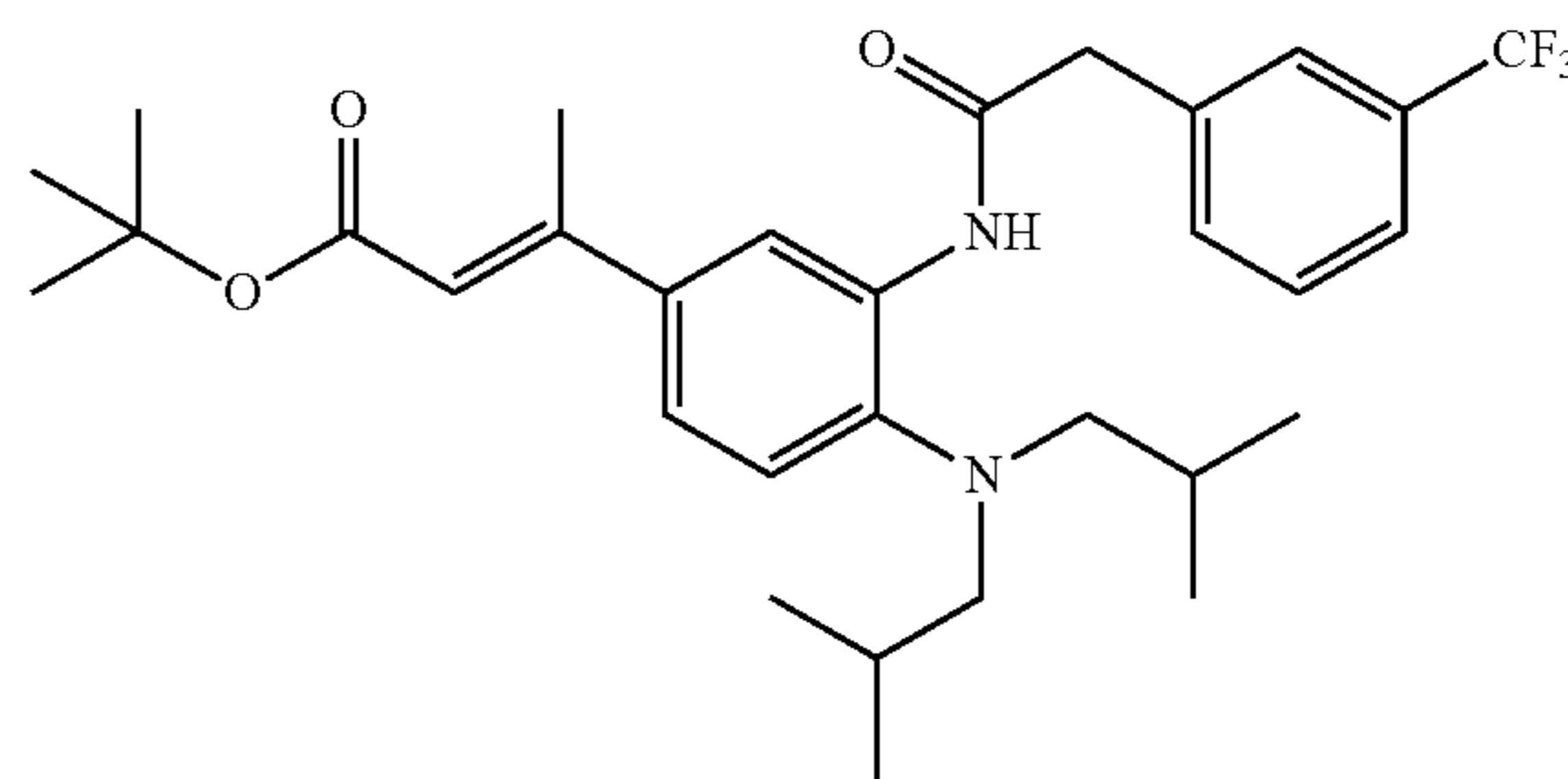
$^1\text{H-NMR}$ (600 MHz, DMSO-d_6) δ 12.30 (s, 1H), 9.22 (s, 1H), 8.06 (s, 1H), 8.01 (s, 11H), 7.88 (t, $J=8.5$ Hz, 1H), 7.47 (d, $J=15.8$ Hz, 1H), 7.28 (d, $J=9.6$ Hz, 1H), 7.18 (d, $J=8.4$ Hz, 1H), 7.07 (d, $J=12.2$ Hz, 1H), 6.95 (d, $J=8.0$ Hz, 1H), 6.30 (d, $J=15.9$ Hz, 1H), 2.80 (d, $J=6.9$ Hz, 4H), 2.27 (s, 3H), 1.71 (dt, $J=13.3, 6.7$ Hz, 2H), 0.82 (d, $J=6.6$ Hz, 12H). MS(ESI), m/z (%): 442.25 $[\text{M}+\text{H}]^+$. White solid.

Compound 1059



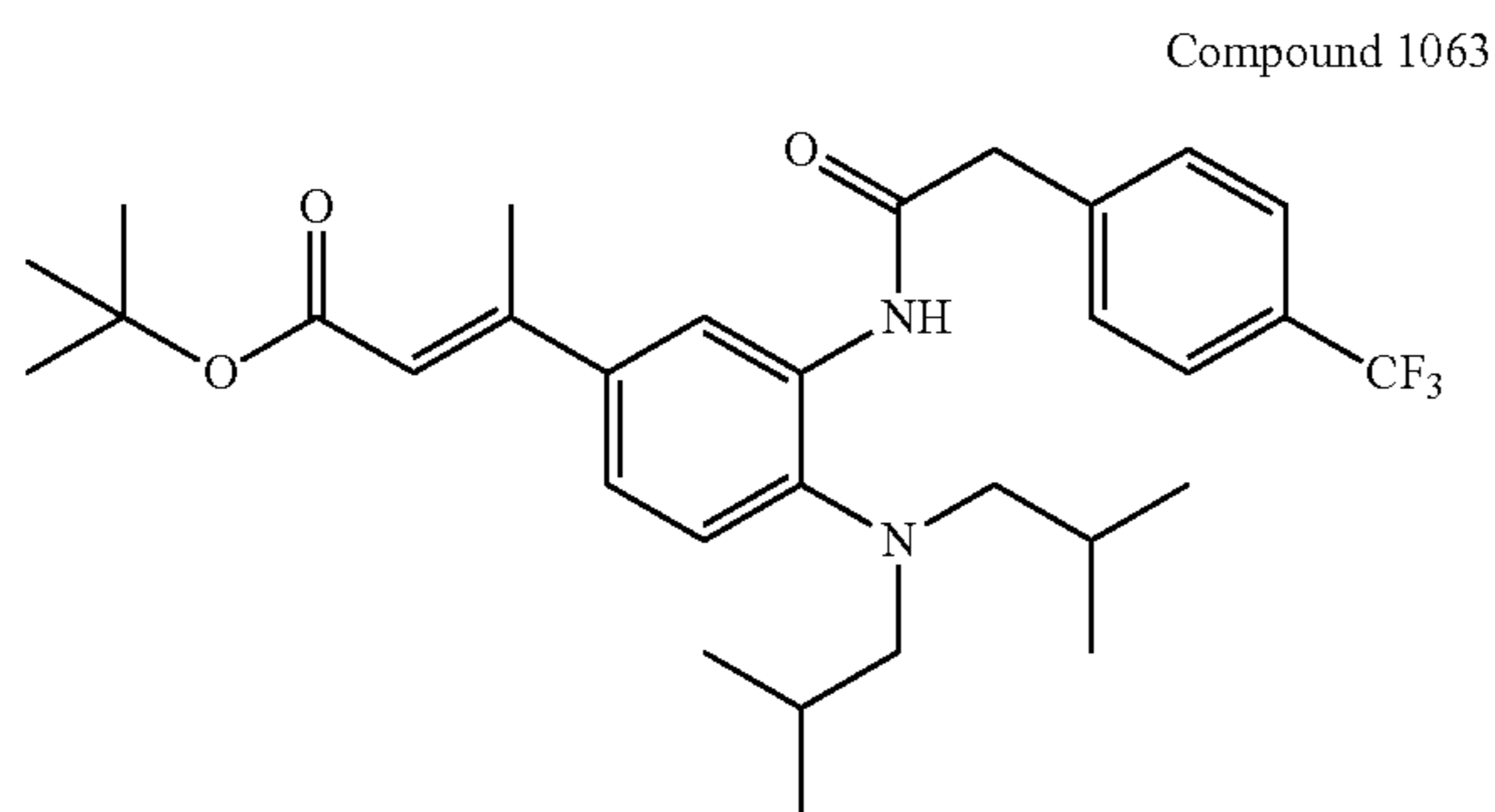
$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.43 (s, 1H), 8.14 (s, 1H), 7.86 (t, $J=8.4$ Hz, 1H), 7.63 (d, $J=16.0$ Hz, 1H), 7.13 (s, 2H), 6.91 (dd, $J=13.5, 10.4$ Hz, 2H), 6.42 (d, $J=16.0$ Hz, 1H), 4.22 (q, $J=7.1$ Hz, 2H), 2.58 (d, $J=7.2$ Hz, 4H), 2.30 (s, 3H), 1.71 (dt, $J=13.5, 6.8$ Hz, 2H), 1.31 (t, $J=7.1$ Hz, 3H), 0.87 (d, $J=6.6$ Hz, 12H). MS(ESI), m/z (%): 470.31 $[\text{M}+\text{H}]^+$. White solid.

Compound 1062



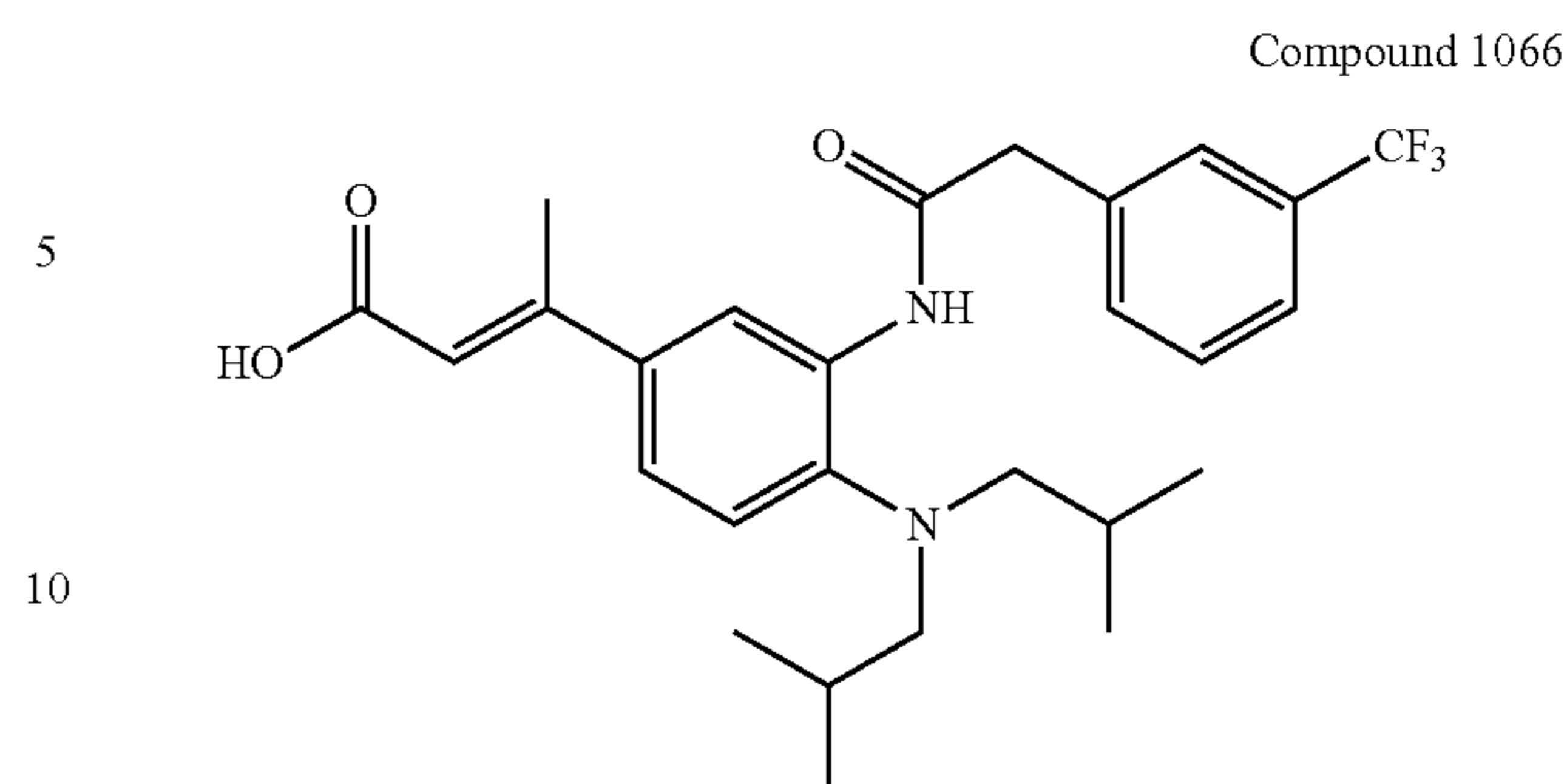
$^1\text{H-NMR}$ (600 MHz, DMSO-d_6) δ 8.81 (s, 1H), 8.24 (s, 1H), 7.73 (s, 1H), 7.66 (s, 1H), 7.59 (s, 1H), 7.56 (s, 1H), 7.51 (s, 11H), 7.26 (d, $J=2.1$ Hz, 1H), 7.24 (s, 1H), 5.97 (s, 1H), 3.91 (s, 2H), 2.61 (d, $J=7.1$ Hz, 4H), 2.44 (s, 3H), 1.60 (dd, $J=13.4, 6.7$ Hz, 2H), 1.46 (s, 9H), 0.77 (d, $J=6.6$ Hz, 12H). MS(ESI), m/z (%): 547.38 $[\text{M}+\text{H}]^+$. White solid.

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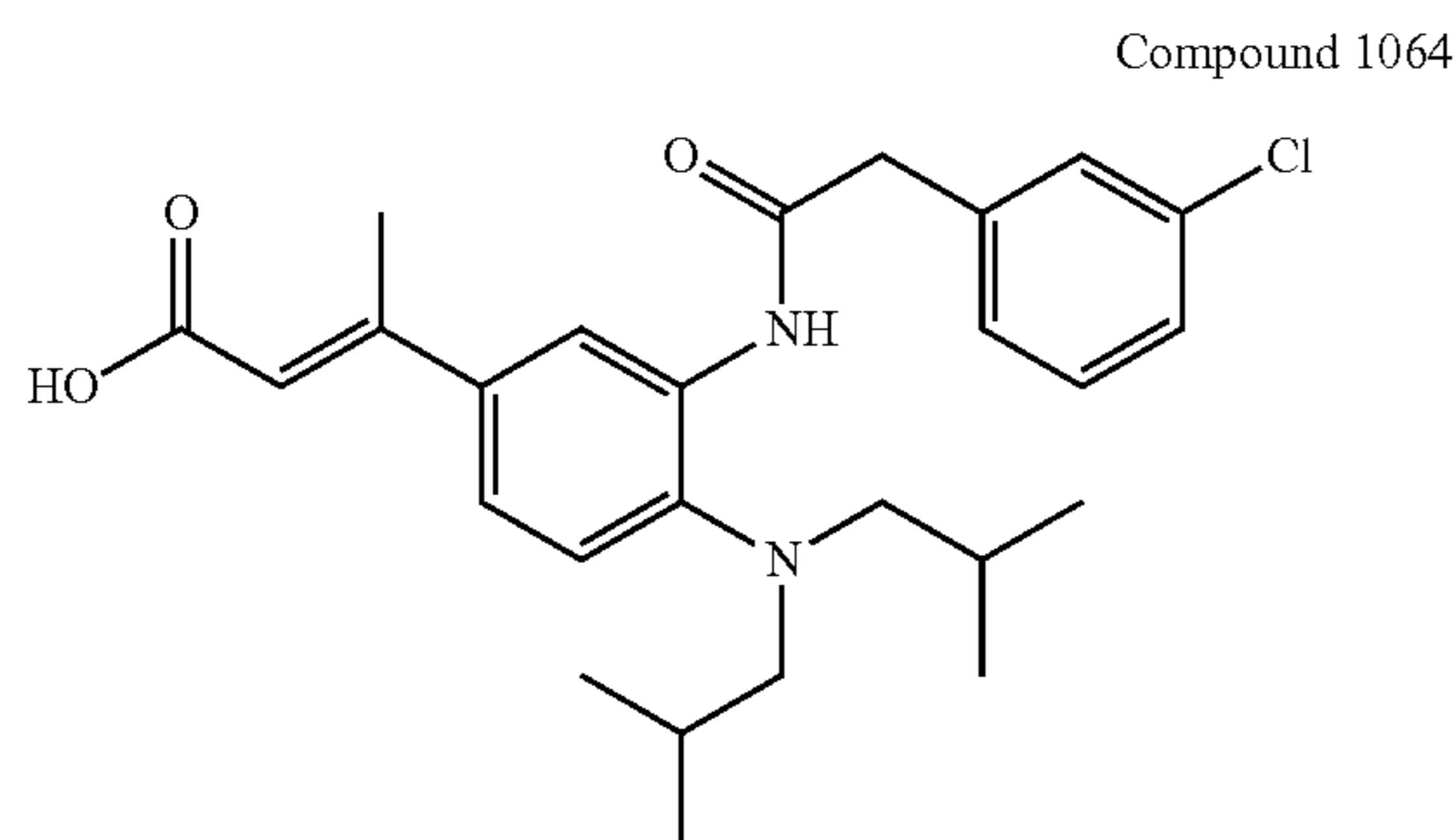
¹H-NMR (600 MHz, DMSO-d₆) δ 8.77 (s, 1H), 8.24 (s, 1H), 7.73 (d, J=1.5 Hz, 1H), 7.66 (s, 2H), 7.51 (d, J=2.7 Hz, 1H), 7.42 (s, 2H), 5.95 (s, 1H), 3.89 (s, 2H), 2.60 (d, J=7.1 Hz, 4H), 2.44 (s, 3H), 1.59 (dd, J=13.3, 6.6 Hz, 2H), 1.46 (s, 9H), 0.76 (d, J=6.6 Hz, 12H). MS(ESI), m/z (%): 547.38 [M+H]⁺. White solid.

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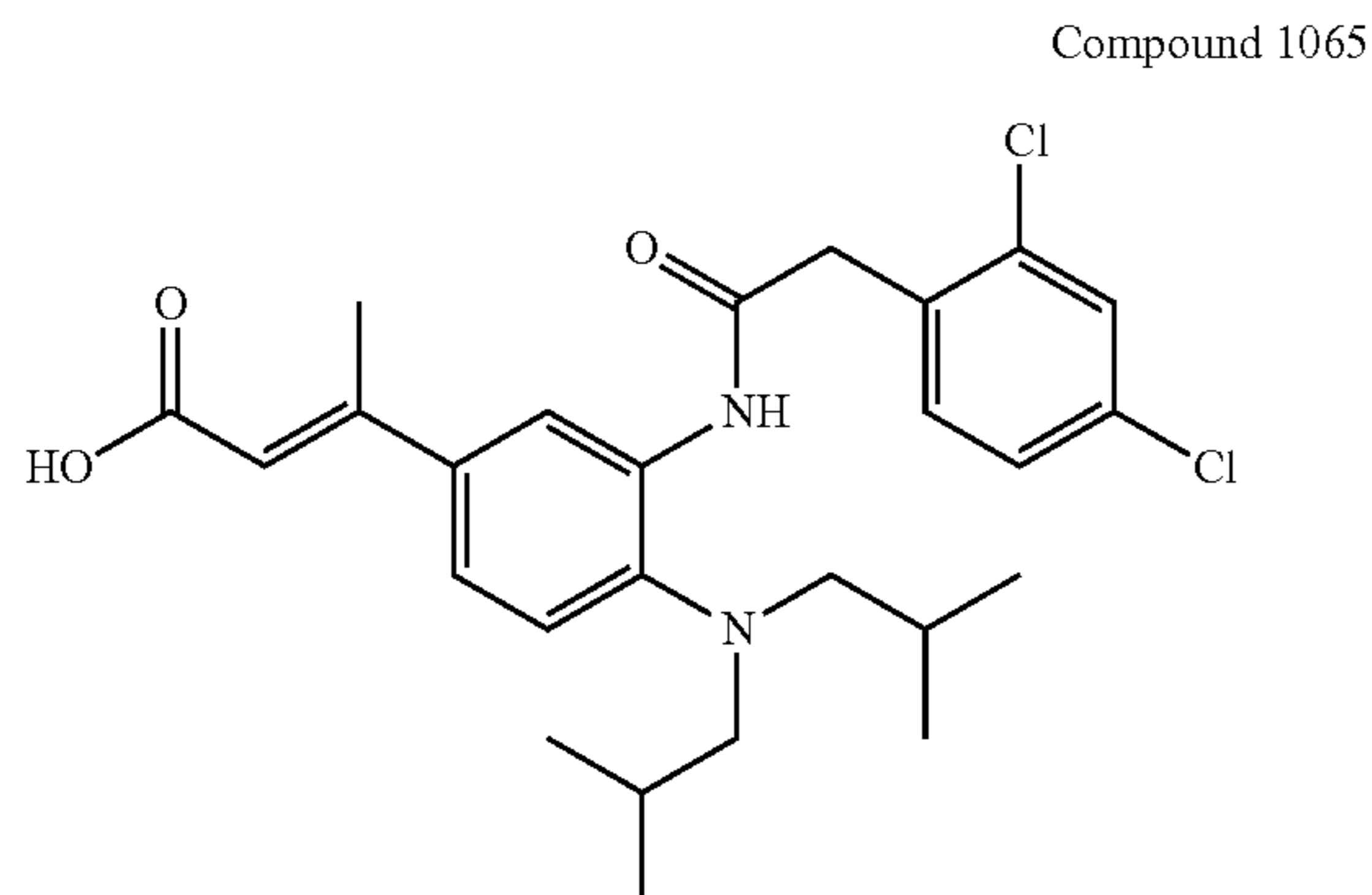


¹H-NMR (600 MHz, DMSO-d₆) δ 12.02 (s, 1H), 8.80 (s, 1H), 8.23 (s, 1H), 7.73 (d, J=3.1 Hz, 1H), 7.68-7.66 (m, 1H), 7.27 (d, J=2.0 Hz, 1H), 7.25 (s, 1H), 7.21 (d, J=8.3 Hz, 1H), 6.93 (d, J=6.7 Hz, 1H), 6.04 (s, 1H), 3.90 (s, 2H), 2.62 (d, J=7.0 Hz, 4H), 2.45 (s, 3H), 1.59 (d, J=4.2 Hz, 2H), 0.76 (d, J=6.6 Hz, 12H). MS(ESI), m/z (%): 491.21 [M+H]⁺. White solid.

Test Method and Results of Inhibition Rate of IDO1 Enzyme in Hela Cells:



¹H-NMR (600 MHz, DMSO-d₆) δ 12.04 (s, 1H), 8.73 (s, 1H), 8.27 (s, 1H), 7.44 (s, 1H), 7.38 (s, 1H), 7.36 (s, 1H), 7.27 (d, J=1.9 Hz, 1H), 7.25 (s, 1H), 6.04 (s, 1H), 3.79 (s, 2H), 2.61 (d, J=7.1 Hz, 4H), 2.45 (s, 3H), 1.60 (dd, J=12.4, 5.8 Hz, 2H), 0.77 (d, J=6.6 Hz, 12H). MS(ESI), m/z (%): 457.26 [M+H]⁺. White solid.



¹H-NMR (600 MHz, DMSO-d₆) δ 12.06 (s, 1H), 8.73 (s, 1H), 8.33 (s, 1H), 7.64 (s, 1H), 7.52 (d, J=8.5 Hz, 1H), 7.46 (s, 1H), 7.28 (s, 2H), 6.04 (s, 1H), 3.92 (s, 2H), 2.64 (d, J=7.1 Hz, 4H), 2.45 (s, 3H), 1.64-1.61 (m, 2H), 0.81 (d, J=6.6 Hz, 12H). MS(ESI), m/z (%): 491.22 [M+H]⁺. White solid.

Human cervical cancer cell line Hela (obtained from Chinese academy of sciences cell bank) was cultured in logarithmic growth phase and counted after routine digestion. RPMI 1640 complete medium (Corning, USA, containing 10% FBS) was used to adjust the concentration to 1x 10⁶/ml, inoculated into 96-well plates, 100 ul/well, incubated for 24 hours.

Stimulant solution configuration: Human recombinant IFN-γ (Shanghai Sangon Biotech) was subpacked according to the instructions, the concentration was adjusted twice as high as the final concentration by RPMI1640 complete medium, that is 100 ng/ml.

Compounds solution configuration: DMSO was used to dissolve the drug, and then RPMI 1640 was used to dilute the drug to twice the detection concentration.

The old culture medium were discarded from 96-well plates, and added 100 ul stimulation solution and 100 ul compounds solution to each hole; set up interferon growth control group, each group had three multiple holes; incubated 48 hours.

180 uL medium from 96-well plate were collected and mixed with 45 μL of 30% (W/V) trichloroacetic acid. Plate was centrifuged for 5 min at 8000 rpm. The supernatant was added with fresh 4-dimethylaminobenzaldehyde (2%, W/V). After full shock, measured at 480 nm using a ELISA reader.

TABLE 7

Inhibition rate of compounds on IDO1 activity enzyme in Hela cells		
Compound Number	Inhibition rate (%)	
	10 μmol	100 nmol
Compound 9	100	100
Compound 13	100	100
Compound 14	100	100
Compound 396	100	69.2
Compound 397	100	75.5
Compound 403	100	76.4
Compound 404	100	73.2
Compound 518	100	76.8
Compound 525	100	75.1
Compound 564	100	72.2
Compound 772	100	74.2
Compound 779	100	77.1

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TABLE 7-continued

Inhibition rate of compounds on IDO1 activity enzyme in Hela cells		
Compound Number	Inhibition rate (%)	
	10 μ mol	100 nmol
Compound 1021	100	42.1
Compound 1022	53.7	21.2
Compound 1023	100	35.1
Compound 1024	58.2	29.5
Compound 1025	68.8	24.6
Compound 1026	54.3	21.0
Compound 1027	100	71.1
Compound 1028	100	41.5
Compound 1030	100	23.8
Compound 1031	72.7	29.6

The compounds described in the above table have certain inhibitory effects, Compounds 9, 13 and 14 can inhibit IDO-1 activity 100% at 100 nmol concentration.

TABLE 8

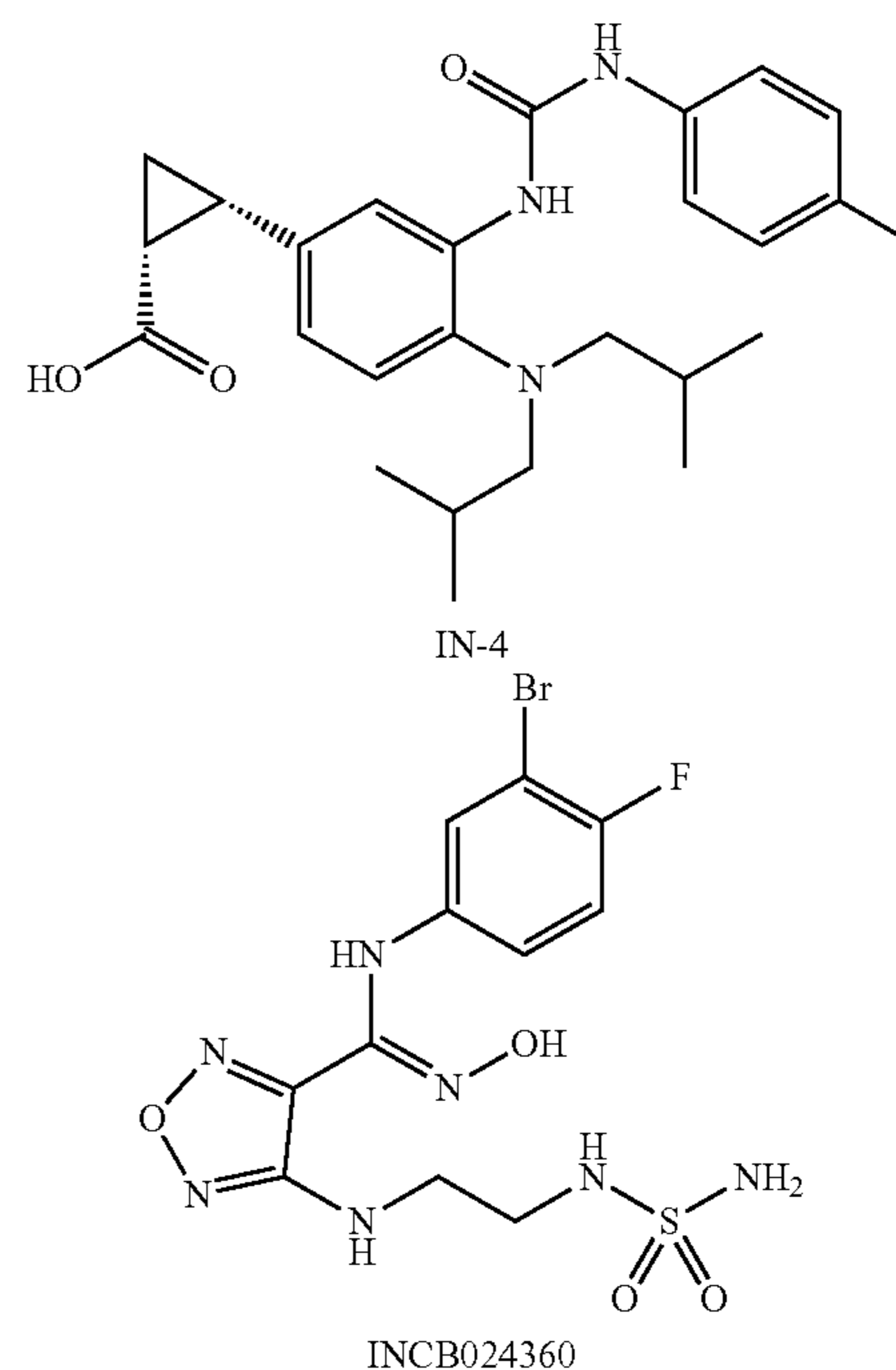
IC ₅₀ Value (nmol/L) of compounds on IDO1 enzyme activity in Hela cells	
Compound Number	Inhibition rate IC ₅₀ (nmol/L)
Compound 13	3.69
Compound 14	0.18
Compound 51	3.69
Compound 55	0.09
Compound 56	0.13
Compound 525	1.36
Compound 530	8.26
INCB024360	3.78
IN-4	1.56

As shown in the table above, the IC₅₀ of the compounds is lower than 100 nmol/L, and the activities of the compounds 525, 13, 14, 56, 55 and 51 can reach or exceed those of the positive control drugs INCB024360 and IN-4, indicating that these compounds have good IDO1 enzyme inhibitory activities.

As shown in Table 7 and Table 8 above, these compounds have potential therapeutic effects on colorectal cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, cervical cancer, renal cancer, head and neck cancer, lymphoma, leukemia or melanoma with high expression of IDO1. It has potential therapeutic effects on other diseases such as viral infection, depression, organ transplant rejection or autoimmunity caused by high expression of IDO1.

INCB024360 control sample was purchased from Beijing Innochem Technology Co., Ltd. with batch number WG0292821-160526001. IN-4 was purchased from Medchem Express Biotechnology Company, USA, with batch number Lot #19346.

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Pharmacokinetic Test and Results of Compound 55:

12 Male Sprague-Dawley rats were grouped random. The final concentration of compound 55 was 1.5 mg/ml. The drug was dissolved in a solvent system of 10% DMSO, 10% hydrogenated castor oil and 90% normal saline (compounds were dissolved by DMSO, hydrogenated castor oil and saline in turn by vortex or ultrasound), and the drug solution was given orally (30 mg/kg). The rats were fasted overnight but had free access to water, feeding resumed 4 hours after administration. Blood samples (0.3-0.4 mL) were collected into heparinized tubes by Retinal vein plexus at 0, 0.17, 0.33, 0.67, 1, 2, 4, 7, 10 and 24 hours after administration orally. Tubes were anticoagulated with heparin sodium (5% heparin sodium solution filled EP tube, poured out, dried). 100 μ L plasma was obtained by centrifugation (10000 rpm, 3 min) and stored at -20° C. before analysis.

TABLE 9

Oral pharmacokinetic data of compound 55		
Testing Compound	Unit	Compound 55
Dosage	mg/kg	30 mg/kg
AUC	ng \cdot h/mL	43655.98
T1/2	h	5.0
Cmax	ng/mL	16760.13

The results showed that compound 55 had good pharmacokinetic parameters.

Pharmacodynamics of Some Compounds In Vivo (Intraperitoneal Injection):

The anti-colon cancer CT26 activity of these compounds was tested in vivo. 1×10^6 CT26 cells were inoculated subcutaneously in the right axillary of BALB/c mice by cell suspension inoculation. When the growth of tumors were clearly observed, 42 moderately tumor size animals were selected and randomly divided into test group, solvent control group and positive drug group, with 6 animals in each group. The positive drug group was given 1-methyl-D-tryptophan 300 mg/kg daily by oral, and the INCB024360

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group was given compound INCB024360 50 mg/kg daily by intraperitoneal injection. The compound groups were intraperitoneally injected with 50 mg/kg of the compound every day, while the solvent control group was given the same dosage with the same volume of mixed solvent. The weight of the mice and the length and short diameter of the transplanted tumors were measured three times a week during the administration. The tumor volume (VT), relative volume (RVT) and tumor proliferation rate (T/C %) were calculated. After two weeks of administration, nude mice bearing tumors in each experimental group were executed by neck-lifting method. Solid tumour tissues were completely dissected. The weight of tumors in each experimental group was measured and the growth inhibition rate (%) was calculated.

TABLE 10

Statistical table of tumor weight and inhibition rate of tumor weight			
Group	Number of animals (n)	Tumor weight (mg)	Inhibition rate (%)
Vehicle	6	3368.00 ± 557.96	0.0
1-MT	6	2509.17 ± 352.16	25.5
INCB024360	6	3026.17 ± 409.75	10.23
Compound 14	6	2727.33 ± 404.42	19.02
Compound 55	6	2121.17 ± 343.15	37.02

At the end of the experiment, the I-MT activity of the positive drug was better than that of INCB024360, and compound 55 was equivalent to that of 1-MT, which was better than that of INCB024360.

Pharmacodynamic of Some Compounds In Vivo (Oral Administration):

The anti-colon cancer CT26 activity of these compounds was tested in vivo. 1×10^6 CT26 cells were inoculated subcutaneously in the right axillary of BALB/c mice by cell suspension inoculation. When the growth of tumors were clearly observed, 56 moderately tumor size animals were selected and randomly divided into test group, solvent control group and positive drug group, with 8 animals in each group. In the positive drug group, INCB024360 was given 50 mg/kg each time, compound 14 was given 50 mg/kg each time, compound 55 low dose group, compound 55 middle dose group and compound 55 high dose group were given 20 mg/kg, 50 mg/kg and 100 mg/kg respectively, compound 55 intraperitoneal injection group was given 50 mg/kg each time. The solvent control group was given the same volume of mixed solvents by oral. The above groups were administered twice a day. The weight of the mice and the length and short diameter of the transplanted tumors were measured three times a week during the administration. The tumor volume (VT), relative volume (RVT) and tumor proliferation rate (T/C %) were calculated. After two weeks of administration, nude mice bearing tumors in each experimental group were executed by neck-lifting method. Solid tumour tissues were completely dissected. The weight of tumors in each experimental group was measured and the growth inhibition rate (%) was calculated.

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TABLE 11

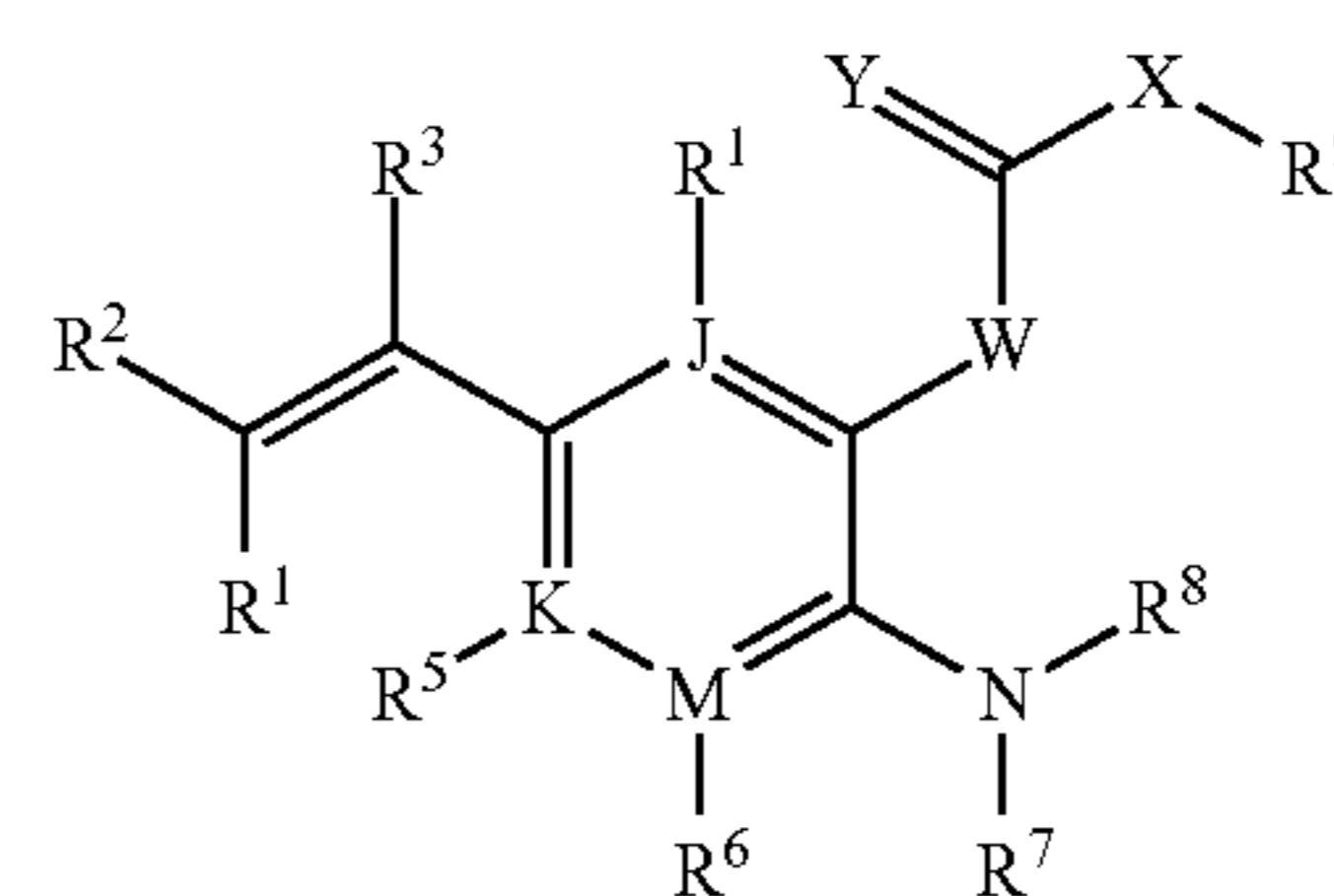
Statistical table of tumor weight and inhibition rate of tumor weight				
Group	Dose (mg/kg)	Number of animals (n)	Tumor weight (mg)	Inhibition rate (%)
Solvent control	—	8	1267.13 ± 331.64	
INCB024360	50	8	840.63 ± 144.34	33.66
Compound 55	20	8	1109.75 ± 191.47	12.42
Compound 55	50	8	924.25 ± 150.35	27.06
Compound 55	100	8	847.00 ± 305.01	33.16
Compound 14	50	8	793.38 ± 246.34	37.39
Compound 55 (IP)	50	8	824.00 ± 161.64	34.97

At the end of the experiment, the activity of compound 55, high dose group and compound 14 was similar to that of positive drug INCB024360.

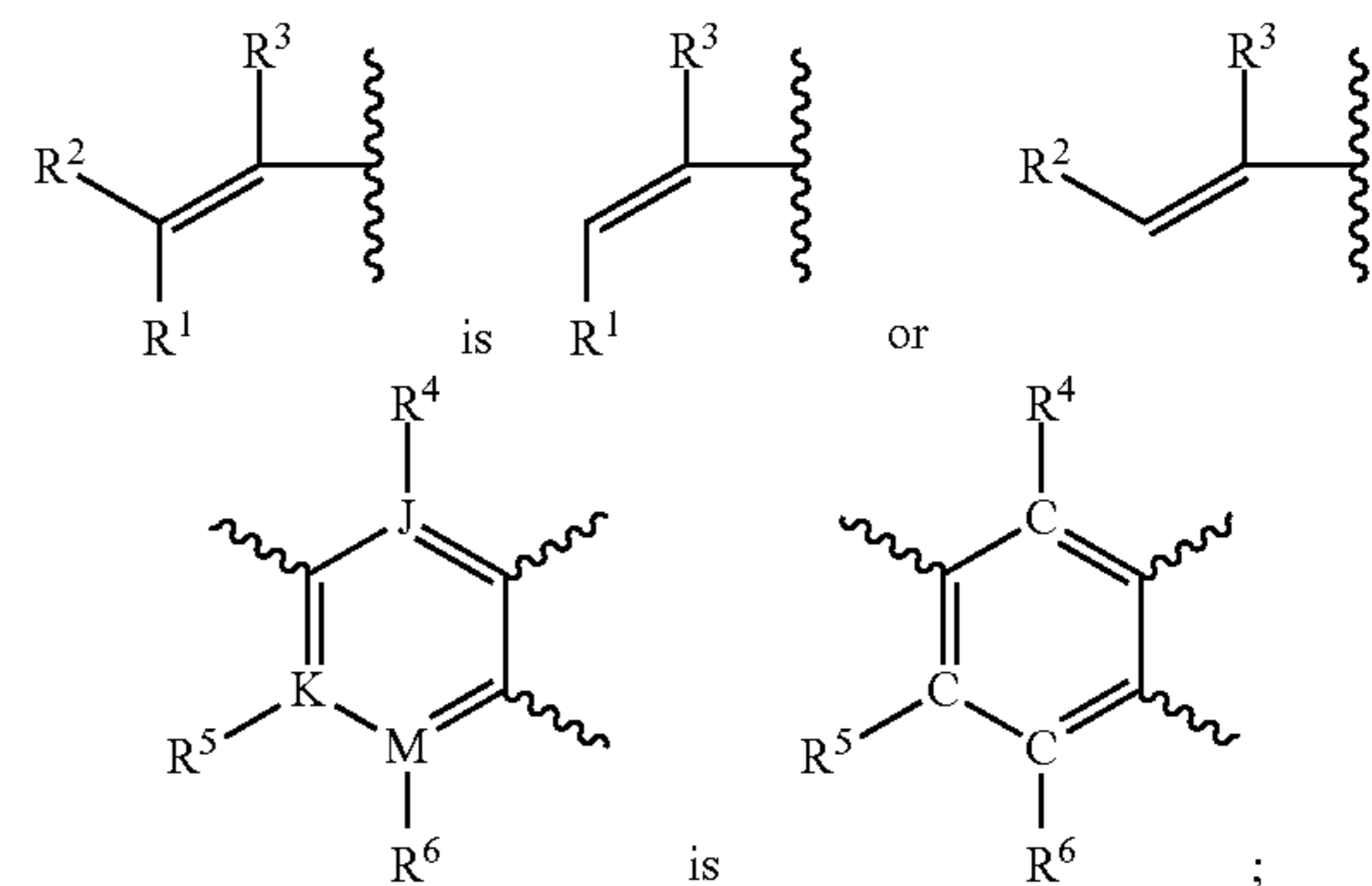
Combining with the previous intraperitoneal injection in vivo pharmacodynamics experiments, compound 55 has better pharmacodynamics than INCB024360 under the condition of single administration per day, and is equivalent to INCB024360 under the condition of twice administration per day. The T1/2 data of INCB024360 reported in the literature were 2.3 hours and that of compound 55 was 5.0 hours. Combining animal pharmacodynamics experiment and pharmacokinetics experiment data, compound 55 has better pharmacokinetic properties than INCB024360, and can achieve considerable pharmacodynamics with fewer times of administration.

We claim:

1. A vinylarene derivative having formula I, its stereoisomer, cis-trans isomer, tautomer and pharmaceutically acceptable salt thereof where formula I includes:



and wherein

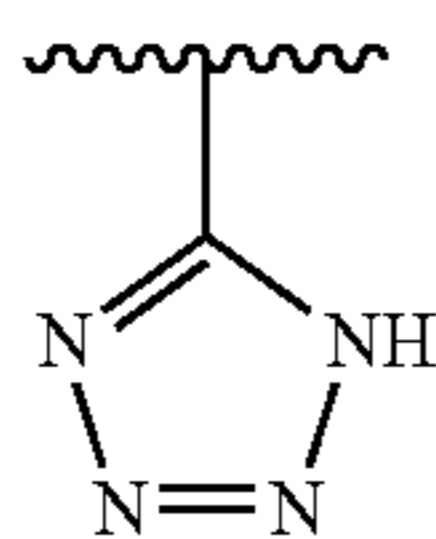


W is NH;
X is NH or CH₂;
Y is O;
J is C;

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K is C;

M is C;

R¹ and R² is selected from COOH,or COOCH₂CH₃;R³ is selected from CH₃;R⁴ is selected from H;R⁵ is selected from H;R⁶ is selected from H;**86**R⁷ and R⁸ are the same or different and selected from n-butyl or isobutyl;

5 R⁹ is selected from 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2,4-dimethylphenyl, 2,4-difluorophenyl, 2-fluoro-4-methylphenyl, 3-trifluoromethyl-4-chlorophenyl, phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,4-dichlorophenyl, 2-fluorophenyl, 4-fluorophenyl, 3-fluorophenyl or 5-methylisoxazolyl.

10 **2.** A treatment method comprising administering to a subject with a cancer selected from colon cancer, pancreatic cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, cervical cancer, kidney cancer, head and neck cancer, lymphoma, leukemia or melanoma an effective amount of the vinylarene derivative described in claim 1.

15 **3.** A pharmaceutical composition comprising an effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier or diluent.

* * * * *